(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
7 February 2002 (07.02.2002)

PCT

(10) International Publication Number
WO 02/10398 A2

(51) International Patent Classification[7]: C12N 15/52, 15/82, A01H 1/00, A01N 65/00 // C12N 15/61

(21) International Application Number: PCT/US01/24037

(22) International Filing Date: 31 July 2001 (31.07.2001)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/221,703 31 July 2000 (31.07.2000) US

(71) Applicants and
(72) Inventors: **HAHN, Frederick, M.** [US/US]; P.O. Box 790429, Kula, HI 96779 (US). **KUEHNLE, Adelheid, R.** [US/US]; 3119 Beaumont Woods Place, Honolulu, HI 96822 (US).

(74) Agents: **LLOYD, Jeff** et al.; Saliwanchik, Lloyd & Saliwanchik, Suite A-1, 2421 N.W. 41st Street, Gainesville, FL 32606 (US).

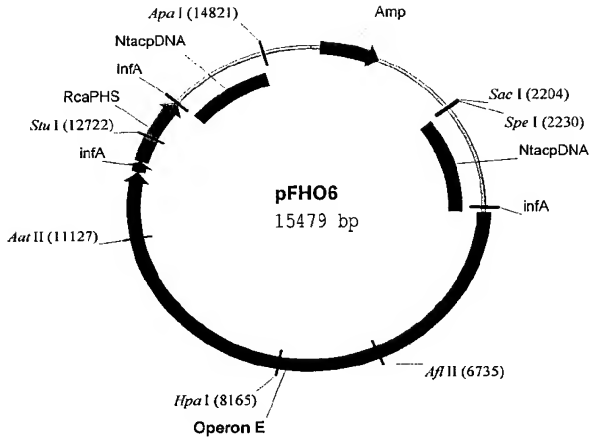
(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CII, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *without international search report and to be republished upon receipt of that report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: MANIPULATION OF GENES OF THE MEVALONATE AND ISOPRENOID PATHWAYS TO CREATE NOVEL TRAITS IN TRANSGENIC ORGANISMS



(57) Abstract: Disclosed are the uses of specific genes of the mevalonate and isoprenoid biosynthetic pathways, and of inactive gene sites (the pseudogene) to (1) enhance biosynthesis of isopentenyl diphosphate, dimethylallyl diphosphate and isoprenoid pathway derived products in the plastids of transgenic plants and microalgae, (2) create novel antibiotic resistant transgenic plants and microalgae, and (3) create a novel selection system and/or targeting sites for mediating the insertion of genetic material into plant and microalgae plastids. The specific polynucleotides to be used, solely or in any combination thereof, are publicly available from GeneBank and contain open reading frames having sequences that upon expression will produce active proteins with the following enzyme activities: (a) acetoacetyl CoA thiolase (EC 2.3.1.9), (b) 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) synthase (EC 4.1.3.5), (c) HMG-CoA reductase (EC 1.1.1.34), (d) mevalonate kinase (EC 2.7.1.36), (e) phosphomevalonate kinase (EC 2.7.4.2), (f) mevalonate diphosphate decarboxylase (EC 4.1.1.33), (g) isopentenyl diphosphate (IPP) isomerase (EC 5.3.3.2), and (b) phytoene synthase (EC 2.5.1.32).

WO 02/10398 A2

DESCRIPTION

MANIPULATION OF GENES OF THE MEVALONATE AND ISOPRENOID PATHWAYS TO CREATE NOVEL TRAITS IN TRANSGENIC ORGANISMS

Cross-Reference to a Related Application

This application claims the benefit of U.S. Provisional Application No. 60/221,703, filed July 31, 2000.

Field of the Invention

This invention relates to the fields of biotechnology and genetic engineering, in particular to agricultural and aquacultural biotechnology. More specifically, the invention relates to transgenic plants and microalgae, in particular to transplastomic plants and microalgae and means for insertion of genetic material into plastids.

Background of the Invention

The ubiquitous isoprenoid biosynthetic pathway is responsible for the formation of the most chemically diverse family of metabolites found in nature (Hahn *et al.*, J. Bacteriol. 178:619-624, 1996) including sterols (Popjak, Biochemical symposium no. 29 (T. W. Goodwin, ed.) Academic Press, New York, pp17-37, 1970), carotenoids (Goodwin, Biochem. J. 123:293-329, 1971), dolichols (Matsuoka *et al.*, J. Biol. Chem. 266:3464-3468, 1991), ubiquinones (Ashby and Edwards, J. Biol. Chem. 265:13157-13164, 1990), and prenylated proteins (Clarke, Annu. Rev. Biochem. 61:355-386, 1992). Biosynthesis of isopentenyl diphosphate (IPP), the essential 5-carbon isoprenoid precursor, occurs by two distinct compartmentalized routes in plants (Lange and Croteau, Proc. Natl. Acad. Sci. USA 96:13714-13719, 1999). In the plant cytoplasm, IPP is assembled from three molecules of acetyl coenzyme A by the well-characterized mevalonate pathway (Lange and Croteau, Proc. Natl. Acad. Sci. USA 96:13714-13719, 1999). However, a recently discovered mevalonate-independent pathway is responsible for the synthesis of IPP in plant chloroplasts (Lichtenthaler *et al.* FEBS Letters 400:271-274, 1997).

Following the synthesis of IPP via the mevalonate route, the carbon-carbon double

bond must be isomerized to create the potent electrophile dimethylally diphosphate (DMAPP). This essential activation step, carried out by IPP isomerase, insures the existence of the two 5-carbon isomers, IPP and DMAPP, which must join together in the first of a series of head to tail condensation reactions to create the essential allylic diphosphates of the isoprenoid pathway (Hahn and Poulter, J. Biol. Chem. 270:11298-11303, 1995). Recently, it was reported that IPP isomerase activity was not essential in *E. coli*, one of many eubacteria containing only the non-mevalonate pathway for the synthesis of both 5-carbon isomers, suggesting the existence of two separate mevalonate-independent routes to IPP and DMAPP (Hahn *et al.*, J. Bacteriol. 181:4499-4504, 1999). Thus, it is unclear whether an IPP isomerase is essential for the synthesis of isoprenoids in plant plastids as well. Regardless of whether IPP isomerase activity is present in plant plastids, the separation by compartmentalization of the two different biosynthetic routes, the mevalonate and deoxyxylulose phosphate pathways (or "non-mevalonate"), for IPP and DMAPP biosynthesis in plants is the fundamental tenet upon which the subject inventions are based.

The synthesis of IPP by the mevalonate pathway (Eisenreich *et al.*, Chemistry and Biology 5:R221-R233, 1998) is cytoplasm based and occurs as follows: The condensation of two acetyl CoA molecules to yield acetoacetyl CoA is catalyzed by acetoacetyl CoA thiolase (EC 2.3.1.9). The addition of another molecule of acetyl CoA to acetoacetyl CoA is catalyzed by 3-hydroxy-3-methylglutaryl-coenzymeA (HMG-CoA) synthase (EC 4.1.3.5) to yield HMG-CoA, which is reduced in the subsequent step to mevalonate by HMG-CoA reductase (EC 1.1.1.34). Mevalonate is phosphorylated by mevalonate kinase (EC 2.7.1.36) to yield phosphomevalonate, which is phosphorylated, by phosphomevalonate kinase (EC 2.7.4.2) to form mevalonate diphosphate. The conversion of mevalonate diphosphate to IPP with the concomitant release of CO2 is catalyzed by mevalonate diphosphate decarboxylase (EC 4.1.1.33).

In organisms utilizing the deoxyxylulose phosphate pathway (aka "non-mevalonate pathway", "methylerythritol phosphate (MEP) pathway", and "Rohmer pathway"), the five carbon atoms in the basic isoprenoid unit are derived from pyruvate and D-glyceraldehyde phosphate (GAP) (Eisenreich *et al.*, 1998). Thus, synthesis of IPP and/or DMAPP by the non-mevalonate route, which occurs in plastids, is as follows: Pyruvate and GAP are condensed to give 1-deoxy-D-xylulose 5-phosphate (DXP) by

DXP synthase (Sprenger *et al.*, Proc. Natl. Acad. Sci. USA 94:12857-12862, 1997). The rearrangement and reduction of DXP to form 2-C-methylerythritol 4-phosphate (MEP), the first committed intermediate in the non-mevalonate pathway for biosynthesis of isoprenoids is catalyzed by DXP reductoisomerase (Kuzuyama *et al.*, Tetrahedron Lett. 39:4509-4512, 1998). MEP is then appended to CTP to form 4-(cytidine 5'-diphospho)-2- C-methyl-D-erythritol (Rohdich *et al.*, Proc. Natl. Acad. Sci. USA 96:11758-11763, 1999), followed by phosphorylation of the C2 hydroxyl group (Lüttgen *et al.*, Proc. Natl. Acad. Sci. USA 97:1062-1067, 2000) and elimination of CMP, to form a 2,4-cyclic diphosphate (Herz *et al.*, Proc. Natl. Acad. Sci. USA 97:2486-2490, 2000). Interestingly, Herz *et al.* reported the possible existence of bifunctional proteins with both YgbP and YgbB activities. Once the remaining steps to the fundamental five-carbon isoprenoid building blocks, IPP and DMAPP, in the non-mevalonate pathway are discovered, they will serve as additional targets for inhibitors with antiobiotic and herbicidal activity.

Since the non-mevalonate pathway is ultimately responsible for the biosynthesis of compounds critical for photosynthesis such as the prenyl side-chain of chlorophylls, which serve as lipophillic anchors for the photoreceptors and the photoprotective carotenoid pigments, any enzyme, gene, or regulatory sequence involved in the biosynthesis of IPP and/or DMAPP can be a potential target for herbicides. For example, the antibiotic fosmidomycin, a specific inhibitor of the enzyme DXP reductoisomerase (Kuzuyama *et al.*, Tetrahedron Lett. 39:7913-7916, 1998) has been shown to have significant herbicidal activity, especially in combination with other herbicides (Kamuro *et al.* "Herbicide" U.S. Patent No. 4,846,872; issued July 11, 1989). The report of an Arabidopsis thaliana albino mutant being characterized as a disruption of the CLA1 gene, later revealed as encoding DXP synthase by Rohmer *et al.* (Lois *et al.*, Proc. Natl. Acad. Sci. USA 95:2105-2110, 1998), also illustrates the potential of non-mevalonate pathway enzymes as targets for compounds with herbicidal activity. Accordingly, one of ordinary skill in the art can readily understand that as additional compounds are discovered exhibiting herbicidal activity based on their effects on the non-mevalonate pathway, those compounds could be used in accord with the teachings herein.

The synthesis of carotenoids from IPP and DMAPP takes place in plant plastids by a genetically- and enzymatically-defined pathway (Cunningham and Gantt, Ann. Rev.

Plant Mol. Biol. 39:475-502, 1998). Enhanced production of carotenoids such as lycopene and ß-carotene in plants is highly desirable due to the reported health benefits of their consumption (Kajiwara *et al.*, Biochem. J. 324:421-426, 1997). Enhanced carotenoid production in plants can also have a dramatic effect on their coloration and be highly desirable to the growers of ornamentals, for example. The IPP isomerase reaction is considered to be a rate-limiting step for isoprenoid biosynthesis (Ramos-Valdivia *et al.*, Nat. Prod. Rep. 6:591-603, 1997). Kajiwara *et al.* reported that the expression of heterologous IPP isomerase genes in a strain of *E. coli* specifically engineered to produce carotenoids resulted in over a 2-fold increase in ß-carotene formation. Recently, it has been reported that expression of an additional gene for DXP synthase in an *E. coli* strain specifically engineered to produce carotenoids also increased the level of lycopene substantially (Harker and Bramley, FEBS Letters 448:115-119, 1999). Increased isoprenoid production also has been shown in bacteria by combining carotenogenic genes from bacteria with an orf encoding IPP isomerase; and was even further enhanced when additionally combined with the dxs gene from the MEP pathway to supply the precursors IPP and DMAPP (Albrecht *et al.* Nature Biotechnology 18: 843- 846, 2000).

Accumulation of one specific isoprenoid, such as beta-carotene (yellow-orange) or astaxanthin (red-orange), can serve to enhance flower color or nutriceutical composition depending if the host is cultivated as an ornamental or as an output crop; and if the product accumulates in the tissue of interest (*i.e.* flower parts or harvestable tissue). In plants, tissue with intrinsic carotenoid enzymes can accumulate ketocarotenoids such as astaxanthin in chromoplasts of reproductive tissues of tobacco by addition of the biosynthetic enzyme beta-carotene ketolase (Mann *et al.*, Nature Biotechnology 18: 888-892, 2000). Astaxanthin is the main carotenoid pigment found in aquatic animals; in microalgae it accumulates in the Chlorophyta such as in species of Haematococcus and Chlamydomonas. Thus, an increase in the essential 5- carbon precursors, IPP and DMAPP, by expression of orfs encoding IPP isomerase and orfs upstream thereof, can feed into the production output of such valuable isoprenoids in organisms other than bacteria.

As a further example of utility, Petunia flower color is usually due to the presence of modified cyanidin and delphinidin anthocyanin pigments to produce shades in red to blue groupings. Recently produced yellow seed-propagated multiflora and grandiflora

petunias obtain their coloration from the presence of beta-carotene, lutein and zeaxanthin carotenoid pigments in combination with colorless flavonols (Nielsen and Bloor, Scienia Hort. 71: 257-266, 1997). Industry still lacks bright yellow and orange clonally propagated trailing petunias. Metabolic engineering of the carotenoid pathway is desired to introduce these colors in this popular potted and bedding plant.

Plant genetic engineering has evolved since the 1980s from arbitrarily located monocistronic insertions into a nuclear chromosome, often subject to multiple copies, rearrangements and methylation, to predetermined sites for defined multicistronic or multigenic operon insertions into a plastid chromosome (plastome), which thus far is thought impervious to typical nuclear gene inactivation. While breeding of crop plants by nuclear genome engineering is nevertheless a proven technology for major agronomic crops and for traits such as herbicide resistance, introgression of genes into the plastome is a highly promising breeding approach for several reasons as described by Bock and Hagemann (Bock and Hagemann, Prog. Bot. 61:76-90, 2000). Of note is the containment of transgenes in the transplastomic plant: Plastids are inherited through the maternal parent in most plant species and thus plastid-encoded transgenes are unable to spread in pollen to non-target species. Therefore plastid engineering can minimize negative impacts of genetically engineered plants. A report on potential transfer by pollen of herbicide resistance into weedy relatives of cultivated crops (Keeler *et al.*, Herbicide Resistant Crops: Agricultural, Economic, Environmental, Regulatory and Technological Aspects, pp. 303-330, 1996) underscores the value of using plastid engineering rather than nuclear engineering for critical production traits such as herbicide resistance. Daniell *et al.* have recently demonstrated herbicide resistance through genetic engineering of the chloroplast genome (Daniell *et al.*, Nat. Biotechnol., 16:345-348, 1998).

Moreover, plastids are the site of essential biosynthetic activity. Although most associate photosynthesis as the primary function of the chloroplast, studies document that the chloroplast is the center of activity for functions involving carbon metabolism, nitrogen metabolism, sulfur metabolism, biochemical regulation, and various essential biosynthetic pathways including amino acid, vitamin, and phytohormone biosynthesis. Crop traits of interest such as nutritional enhancement require genetic manipulations that impact plastid biosynthetic pathways such as carotenoid production. While nuclear-encoded gene products can be exported from the engineered nucleus into the

plastid for such manipulations, the biosynthetic genes themselves can be inserted into the plastid for expression and activity. As we begin to pyramid multiple genes often required for pathway manipulations (such as the aforementioned carotenoid biosynthesis) the repeated use of selection markers is expected to lead to unstable crops through homology-dependent gene silencing (Meyer and Saedler, Ann. Rev. Plant. Physiol. Mol. Biol. 47:23-48, 1996). In addition, the requirement for higher expression levels of transgenes for effective phenotypes such as vitamin levels and herbicide and pest resistance levels often falls short in nuclear transformations. These deficiencies are overcome through plastid transformation or combining plastid with nuclear transformations: The plastid recognizes strings of genes linked together in multicistronic operons and, due to the high copy number of genes within a plastid and within plastids in a cell, can produce a hundred- to thousand-fold the amount of transgene product. Accordingly, there is a continuing need for improved methods of producing plants having transformed plastids (transplastomic plants).

Golden rice is one example for which plastid engineering can complement nuclear engineering of pathways that reside in the plastid, yet have met with limited success. The metabolic pathway for beta-carotene (pro-vitamin A) was assembled in rice plastids by introduction into the nuclear genome of four separate genes, three encoding plastid-targeted proteins using three distinct promoters, plus a fourth selectable marker gene using a repeated promoter (Ye *et al.* Science 287:303-305, 2000). The wild-type rice endosperm is free of carotenoids but it does produce geranylgeranyl diphosphate; combining phytoene synthase, phytoene desaturase, and lycopene-beta cyclase resulted in accumulation of beta-carotene to make "golden rice". However, the quantity produced was lower than the minimum desired for addressing vitamin A deficiency. An increased supply of precursors for increasing intermediates, such as geranylgeranyl diphosphate, is predicted to significantly increase isoprenoid production. Insertion of an operon encoding the entire mevalonate pathway into the rice plastome of the "golden rice" genotype, using for example the methods as described in Khan and Maliga, Nature Biotechnology 17: 910-914, 1999, can provide a means for making improvements in metabolic engineering of this important monocot crop.

Proplastid and chloroplast genetic engineering have been shown to varying degrees of homoplasmy for several major agronomic crops including potato, rice, maize, soybean,

grape, sweet potato, and tobacco including starting from non-green tissues. Non-lethal selection on antibiotics is used to proliferate cells containing plastids with antibiotic resistance genes. Plastid transformation methods use two plastid-DNA flanking sequences that recombine with plastid sequences to insert chimeric DNA into the spacer regions between functional genes of the plastome, as is established in the field (see Bock and Hagemann, Prog. Bot. 61:76-90, 2000, and Guda *et al.*, Plant Cell Reports 19:257-262, 2000, and references therein).

Antibiotics such as spectinomycin, streptomycin, and kanamycin can shut down gene expression in chloroplasts by ribosome inactivation. These antibiotics bleach leaves and form white callus when tissue is put onto regeneration medium in their presence. The bacterial genes *aad*A and *neo* encode the enzymes aminoglycoside-3′-adenyltransferase and neomycin phosphotransferase, which inactivate these antibiotics, and can be used for positive selection of plastids engineered to express these genes. Polynucleotides of interest can be linked to the selectable genes and thus can be enriched by selection during the sorting out of engineered and non-engineered plastids. Consequently, cells with plastids engineered to contain genes for these enzymes (and linkages thereto) can overcome the effects of inhibitors in the plant cell culture medium and can proliferate, while cells lacking engineered plastids cannot proliferate. Similarly, plastids engineered with polynucleotides encoding enzymes from the mevalonate pathway to produce IPP from acetyl CoA in the presence of inhibitors of the non-mevalonate pathway can overcome otherwise inhibitory culture conditions. By utilizing the polynucleotides disclosed herein in accord with this invention, an inhibitor targeting the non-mevalonate pathway and its components can be used for selection purposes of transplastomic plants produced through currently available methods, or any future methods which become known for production of transplastomic plants, to contain and express said polynucleotides and any linked coding sequences of interest.

This selection process of the subject invention is unique in that it is the first selectable trait that acts by pathway complementation to overcome inhibitors. This is distinguished from the state of the art of selection by other antibiotics to which resistance is conferred by inactivation of the antibiotic itself, *e.g.* compound inactivation as for the aminoglyoside 3'-adenyltransferase gene or neo gene. This method avoids the occurrence of resistant escapes due to random insertion of the resistance gene into the nuclear

genome or by spontaneous mutation of the ribosomal target of the antibiotic, as is known to occur in the state of the art. Moreover, this method requires the presence of an entire functioning mevalonate pathway in plastids. For example, if one of the enzyme activities of the mevalonate pathway is not present in the plastid, resistance will not be conferred.

There is strong evidence indicating that the origin of plastids within the cell occurred via endosymbiosis and that plastids are derived from cyanobacteria. As such, the genetic organization of the plastid is prokaryotic in nature (as opposed to the eukaryotic nuclear genome of the plant cell). The plastid chromosome ranges from roughly 110 to 150 Kb in size (196 for the green alga Chlamydomonas), much smaller than that of most cyanobacteria. However, many of the bacterium genes have either been lost because their function was no longer necessary for survival, or were transferred to the chromosomes of the nuclear genome. Most, but not all, of the genes remaining on the plastid chromosome function in either carbon metabolism or plastid genetics. However, many genes involved in these functions, as well as the many other functions and pathways intrinsic to plastid function, are also nuclear encoded, and the translated products are transported from the cytoplasm to the plastid. Studies have documented nuclear encoded genes with known activity in the plastid that are genetically more similar to homologous genes in bacteria rather than genes of the same organism with the same function but activity in the cytoplasm as reviewed for example in Martin *et al.* (1998) Nature 393:162-165 and references therein.

The process whereby genes are transported from the plastid to the nucleus has been addressed. Evidence indicates that copies of many plastid genes are found among nuclear chromosomes. For some of these, promoter regions and transit peptides (small stretches of DNA encoding peptides that direct polypeptides to the plastid) become associated with the gene that allows it to be transcribed, and the translated polypeptide relocated back into the plastid. Once this genetic apparatus has become established, the genes present in the plastid chromosome may begin to degrade until they are no longer functional, *i.e.*, any such gene becomes a pseudogene.

As is common in prokaryotic systems, many genes that have a common function are organized into an operon. An operon is a cluster of contiguous genes transcribed from one promoter to give rise to a polycistron mRNA. Proteins from each gene in the polycistron are then translated. There are 18 operons in the plastid chromosome of

tobacco (Nicotiana tabacum). Although many of these involve as few as two genes, some are large and include many genes. Evolutionary studies indicate that gene loss- as pseudogenes or completely missing sequences- occurs as individuals rather than as blocks of genes or transcriptional units. Thus other genes surrounding a pseudogene in a polycistronic operon remain functional.

The rpl23 operon consists of genes whose products are involved in protein translation. Most of these genes are ribosomal proteins functioning in either the large or small ribosomal subunit. One particular gene of note, infA, encodes an initiation factor protein that is important in initiating protein translation. Although this gene is functional in many plants, it is a pseudogene in tobacco and all other members of that family (Solanaceae), including the horticulturally valuable tomato, petunia, and potato crops. A recent survey of plant groups has indicated that there have been numerous loses of functionality of infA (Millen *et al.*, Plant Cell 13: 645-658, 2001). This as well as other pseudogenes are identified in species whose chloroplast genomes have not yet been fully sequenced.

Pseudogenes such as infA become potential target sequences for insertion of intact orfs. Inserted orfs are controlled by regulatory upstream and downstream elements of the polycistron and are promoterless themselves. Pseudogenes are known for a multiplicity of crops and algae with chloroplast genomes that are already fully sequenced. Crops include grains such as rice and trees such as Pinus. Of note in the latter are the eleven ndh genes; all may serve as potential targets for transgene insertion.

Transplastomic solanaceous crops are highly desirable in order to eliminate the potential for gene transfer from engineered lines to wild species, as demonstrated in Lycopersicon (Dale, P.J. 1992. Spread of engineered genes to wild relatives. Plant Physiol. 100:13-15.). A method for plastid engineering that enables altered pigmentation, for improved nutrition in tomato or improved flower color in Petunia and ornamental tobacco as examples, is desirable for solanaceous crops. The infA gene is widely lost among rosids and some asterids; among the latter, infA is a pseudogene in all solanaceous species examined (representing 16 genera). The solanaceous infA DNA sequences show high similarity, with all nucleotide changes within infA being documented. Thus one set of flanking sequences of reasonable length as known in the art should serve for directed insertion of an individual or multiple orfs into the infA sites of the solanaceous species.

It is documented in a solanaceous species that flanking sequences for genes to be inserted into the plastome are not required to be specific for the target species, as incompletely homologous plastid sequences are integrated at comparable frequencies (Kavanagh *et al.*, Genetics 152:1111-1122, 1999).

The upstream 5' region, often referred to as the 5' UTR, is important on the expression level of a transcript as it is translated. Knowing the translation products of surrounding genes in a polycistron allows one to select a pseudogene site that is affiliated with a strong 5' UTR for optimizing plastid expression in a particular tissue. The plastid genome in many plant species can have multiple pseudogenes that are located in different polycistronic sites. So, if one has a choice, one can select a site based on whether it is actively transcribed in green vs non-green plastid; and then if the polycistron has high or low relative expression in that plastid type. Moreover, monocistronic mRNA of ndhD was detected in developed leaves but not in greening or expanding leaves of barley (Hordeum vulgare), despite this gene being part of a polycistronic unit as reported by del Campo *et al.* (1997) Plant Physiol 114:748. Thus, one can time transgene product production by treating an inactive gene, based on developmental expression, as a pseudogene for targetting and integration purposes using the invention disclosed herein.

Algal species are becoming increasingly exploited as sources of nutraceuticals, pharmaceuticals, and lend themselves to aquaculture. Mass production of the isoprenoid compound astaxanthin produced by the green microalga Haemotcoccus is one successful example of the above. Metabolic engineering that would increase product yields and composition in microalgae would significantly benefit the industry. The development of organellar transformation for the unicellular green alga *Chlamydomonas reinhardtii*, with its single large chloroplast, opens the door for conducting studies on genetic manipulation of the isoprenoid pathway. Filamentous or multicellular algae are also of interest as untapped biofactories, as are other nongreen algae whose pathways for producing unique fatty acids, amino acids, and pigments can be ameliorated for commercial benefit.

The biolistic DNA delivery method is a general means with which to transform the chloroplast of algae (Boynton and Gillham, Methods Enzymol. 217:510-536, 1993). Sequencing of at least six plastomes from algae should facilitate transformation systems by confirming insertion sites, including pseudogene sites, and the regulatory elements directing heterologous gene expression. What is required is a dominant marker for

selection of stable transformants to which natural resistance is absent (Stevens and Purton, J. Phycol 33: 713-722, 1997). For Chlamydomonas, chloroplasts can be engineered using markers that confer spectinomycin resistance following their integration into the plastome via homologous recombination. By utilizing the polynucleotides disclosed herein in accord with this invention, an inhibitor targeting the non-mevalonate pathway and its components can be used for selection purposes of transplastomic algae produced through currently available methods, or any future methods which become known for production of transplastomic algae, to contain and express said polynucleotides and any linked coding sequences of interest. This is a novel selection vehicle for transplastomic algae. Moreover, elevating the supply of essential precursors for isoprenoid production in algae as described above is enabled by this invention.

Summary of the Invention

This invention relates to the presence of enzymatic activities necessary to form IPP from acetyl CoA, generally known as the mevalonate pathway, within plant and microalgae plastids. This invention may also require the presence of IPP isomerase activity within plastids resulting from the insertion into said plants and microalgae of a polynucleotide encoding a polypeptide with IPP isomerase activity. This invention may be achieved by the use of any polynucleotide, be it a DNA molecule or molecules, or any hybrid DNA/RNA molecule or molecules, containing at least one open reading frame that when expressed provides a polypeptide(s) exhibiting said activities within plastids. These open reading frames may be identical to their wild type progenitors, or alternatively may be altered in any manner (for example, with plastid-optimized codon usage), may be isolated from the host organism to be modified, may originate from another organism or organisms, or may be any combination of origin so long as the encoded proteins are able to provide the desired enzymatic activity within the target plastids. The described open reading frames may be inserted directly into plastids using established methodology or any methodology yet to be discovered. Alternatively, plastid localization of the desired activities may be achieved by modifying genes already residing in the cell nucleus, inserting foreign polynucleotides for nuclear residence, or inserting polynucleotides contained on exogenous, autonomous plasmids into the cell cytoplasm so that in all cases their encoded proteins are transported into the plastid. For example, a chloroplast transit

(targeting) peptide can be fused to a protein of interest. Any combination of the above methods for realizing said activities in plant and microalgae plastids can be utilized. By causing the complete mevalonate pathway enzymatic activity to occur in plastids normally possessing only the non-mevalonate pathway, the presence of said activities within the chloroplasts of a specific plant or microalgae will endow it with resistance to a compound, molecule, etc. that targets a component of the non-mevalonate pathway, be it an enzyme, gene, regulatory sequence, etc., thereby also providing a useful selection system based on circumvention of the inhibition of the non-mevalonate pathway in transplastomic plants and microalgae.

In addition, this invention relates to the use of open reading frames encoding polypeptides with enzymatic activities able to convert acetyl CoA to IPP, generally known as the mevalonate pathway, and a polypeptide with IPP isomerase activity as a method for increasing the production of IPP, DMAPP, and isoprenoid pathway derived products whose level within plant and microalgae plastids is dependent on the level of IPP and/or DMAPP present within the plastids. The presence of exogenous genes encoding 1-deoxy-D-xylulose-5-phosphate synthase and IPP isomerase have been shown to increase the production of carotenoids in eubacteria, presumably due to an increased production of IPP and/or DMAPP. Thus, insertion of the entire mevalonate pathway, solely or coupled with an additional IPP isomerase, into plastids will increase the level of IPP and/or DMAPP, resulting in an increased level of carotenoids and other yet to be determined isoprenoid pathway derived products within plant and microalgae plastids. This invention can utilize an open reading frame encoding the enzymatic activity for IPP isomerase independently or in addition to said open reading frames comprising the entire mevalonate pathway to obtain the increased level of isoprenoid pathway derived products within plant and microalgae plastids. This invention may be achieved by the use of any DNA molecule or molecules, or any hybrid DNA/RNA molecule or molecules, containing open reading frames able to provide said activities within plant and microalgae plastids. These open reading frames may be identical to their wild type progenitors, may be altered in any manner, may be isolated from the plant to be modified, may originate from another organism or organisms, or may be any combination of origin so long as the encoded proteins are able to provide said activities within plastids. The described open reading frames may be inserted directly into plant and microalgae plastids using

established methodology or any methodology yet to be discovered. Alternatively, plastid localization of the desired activities may be achieved by modifying genes already residing in the nucleus, inserting foreign genes for nuclear residence, or inserting genes contained on exogenous, autonomous plasmids into the cytoplasm so that in all cases their encoded proteins are transported into the plastid. Any combination of the above methods for realizing said activities in plastids can be utilized.

Further, this invention also relates to the direct insertion of any foreign gene into a plant or microalgae chloroplast by coupling it to the open reading frames encoding polypeptides with enzymatic activities able to convert acetyl CoA to IPP, thus comprising the entire mevalonate pathway. By utilizing a compound, molecule, etc. that targets a component of the non-mevalonate pathway be it an enzyme, gene, regulatory sequence, etc., a method of selection analogous to the use of kanamycin and spectinomycin resistance for the transformation event is achieved. As inhibition of the non-mevalonate pathway in a plant or microalgae results in the impairment of photosynthesis, the presence of the mevalonate pathway biosynthetic capability is apparent, thus enabling the facile screening of concomitant incorporation into plastids of a foreign gene coupled to the open reading frames comprising the entire mevalonate pathway. The use of a polynucleotide comprising an open reading frame encoding a polypeptide with IPP isomerase activity in addition to the open reading frames encoding the mevalonate pathway is a particularly preferred embodiment, which provides all enzymatic activities necessary to synthesize both IPP and DMAPP and overcome the effect(s) of inhibition of the non-mevalonate pathway.

Further, this invention is unique and novel in that the transforming DNA, that is integrated by two or more homologous/heterologous recombination events, is purposefully targeted into inactive gene sites selected based on prior knowledge of transcription in plastid type, developmental expression including post-transcriptional editing, and post-transcriptional stability. Additionally, this invention uses the regulatory elements of known inactive genes (pseudogenes) to drive production of a complete transforming gene unrelated to the inserted gene site. Thus, by utilizing the transgene insertion method disclosed herein in accord with this invention, any foreign gene can be targeted to an inactive gene site (the pseudogene) through currently available methods of gene transfer, or any future methods which become known for production of transgenic

and transplastomic plants, to contain and express said foreign gene and any linked coding sequences of interest. This gene insertion process of the subject invention is unique in that it is the first method specifically acting by pseudogene insertion to overcome the need for promoters and other regulatory elements normally associated with a transforming DNA vector while permitting site-specific recombination in organellar genomes. The use of the infA pseudogene insertion site in the solanaceous crops in particular is a preferred embodiment for the transformation of plastids using the open reading frames for the mevalonate pathway as well as for providing the necessary precursors for modified output traits in plants.

Brief Description of the Drawings

FIG. 1 is a map of cloning vector pFCO1 containing *S. cerevisiae* orfs encoding phosphomevalonate kinase (PMK), mevalonate kinase (MVK), and mevalonate diphosphate decarboxylase (MDD).

FIG. 2 is a map of expression vector pFCO2 containing *S. cerevisiae* orfs encoding phosphomevalonate kinase (PMK), mevalonate kinase (MVK), and mevalonate diphosphate decarboxylase (MDD).

FIG. 3 is a map of cloning vector pHKO1 containing *S. cerevisiae* orf encoding acetoacetyl thiolase (AACT); *A. thaliana* orfs encoding HMG-CoA synthase (HMGS), HMG-CoA reductase (HMGRt).

FIG. 4 is a map of expression vector pHKO2 containing *S. cerevisiae* orfs encoding phosphomevalonate kinase (PMK), mevalonate kinase (MVK), mevalonate diphosphate decarboxylase (MDD), and acetoacetyl thiolase (AACT); *A. thaliana* orfs encoding HMG-CoA synthase (HMGS), HMG-CoA reductase (HMGRt) which in their summation are designated Operon A, encoding the entire mevalonate pathway.

FIG. 5 is a map of cloning vector pHKO3 containing *S. cerevisiae* orfs encoding phosphomevalonate kinase (PMK), mevalonate kinase (MVK), mevalonate diphosphate decarboxylase (MDD), and acetoacetyl thiolase (AACT); *A. thaliana* orfs encoding HMG-CoA synthase (HMGS), HMG-CoA reductase (HMGRt) which in their summation are designated Operon B, encoding the entire mevalonate pathway.

FIG. 6 is an illustration of how the mevalonate (MEV) pathway, by providing an alternative biosynthetic route to IPP, circumvents blocks in the MEP pathway due to a

mutation in the gene for deoxyxylulose phosphate synthase (dxs) and due to inhibtion by fosmidomycin of deoxyxylulose phosphate reductoisomerase (dxr).

FIG. 7 is a map of vector pBSNT27 containing *N. tabcum* chloroplast DNA (cpDNA) and the *N. tabcum infA* pseudogene and pBSNT27 sequence (SEQ ID NO: 17)

FIG. 8 is a map of plastid transformation vector pHKO4 containing *N. tabcum* chloroplast DNA (cpDNA) flanking the insertion of Operon B into the *infA* pseudogene.

FIG. 9 is a map of cloning vector pHKO5 containing *S. cerevisiae* orfs encoding phosphomevalonate kinase (PMK), mevalonate kinase (MVK), and mevalonate diphosphate decarboxylase (MDD), and acetoacetyl thiolase (AACT); *A. thaliana* orfs encoding HMG-CoA synthase (HMGS), HMG-CoA reductase (HMGRt); *R. capsulatus* orf encoding IPP isomerase (IPPI) which in their summation are designated Operon C, encoding the entire mevalonate pathway and IPP isomerase.

FIG. 10 is a map of cloning vector pFHO1 containing *S. cerevisiae* orf encoding acetoacetyl thiolase (AACT); *A. thaliana* orf encoding HMG-CoA synthase (HMGS); *Streptomyces* sp CL190 orf encoding HMG-CoA reductase (HMGR).

FIG. 11 is a map of cloning vector pFHO2 containing *S. cerevisiae* orfs encoding phosphomevalonate kinase (PMK), mevalonate kinase (MVK), and mevalonate diphosphate decarboxylase (MDD), and acetoacetyl thiolase (AACT); *A. thaliana* orf encoding HMG-CoA synthase (HMGS); *Streptomyces sp* CL190 orf encoding HMG-CoA reductase (HMGR) which in their summation are designated Operon D, encoding the entire mevalonate pathway.

FIG. 12 is a map of cloning vector pFHO3 containing *S. cerevisiae* orfs encoding phosphomevalonate kinase (PMK), mevalonate kinase (MVK), and mevalonate diphosphate decarboxylase (MDD), and acetoacetyl thiolase (AACT); *A. thaliana* orf encoding HMG-CoA synthase (HMGS); *Streptomyces sp* CL190 orf encoding HMG-CoA reductase (HMGR); *R. capsulatus* orf encoding IPP isomerase (IPPI) which in their summation are designated Operon E, encoding the entire mevalonate pathway and IPP isomerase.

FIG. 13 is a map of cloning vector pFHO4 containing a *S. cerevisiae* orf encoding acetoacetyl thiolase (AACT) coupled to the *Streptomyces sp* CL190 gene cluster which in their summation are designated Operon F, encoding the entire mevalonate pathway and IPP isomerase.

FIG.14 is is a plastid transformation vector pHKO7 containing *N. tabacum* chloroplast DNA (cpDNA) flanking the insertion of Operon C into the *inf*A pseudogene.

FIG. 15 is a map of expression vector pHKO9 containing Operon B.

FIG. 16 is a map of expression vector pHK10 containing Operon C.

FIG 17 is a map of plastid transformation vector pFHO6 containing *N. tabacum* chloroplast DNA (cpDNA) flanking the insertion of both Operon E and the R. capsulatus orf encoding phytoene synthase (PHS) into the *inf*A pseudogene.

Brief Description of the Sequences

SEQ ID NO: 1) is a PCR primer containing *Saccharomyces cerevisiae* DNA.

SEQ ID NO: 2) is a PCR primer containing S. cerevisiae DNA.

SEQ ID NO: 3) is a PCR primer containing *S. cerevisiae* DNA.

SEQ ID NO: 4) is a PCR primer containing *S. cerevisiae* DNA.

SEQ ID NO: 5) is a PCR primer containing S. cerevisiae DNA.

SEQ ID NO: 6) is a PCR primer containing S. cerevisiae DNA.

SEQ ID NO: 7) is a PCR primer containing Arabidopsis thalian.a DNA.

SEQ ID NO: 8) is a PCR primer containing A. thaliana DNA.

SEQ ID NO: 9) is a PCR primer containing A. thaliana DNA.

SEQ ID NO: 10) is a PCR primer containing *A. thaliana* DNA.

SEQ ID NO: 11) is a PCR primer containing *S. cerevisiae* DNA.

SEQ ID NO: 12) is a PCR primer containing *S. cerevisiae* DNA.

SEQ ID NO: 13) is a Oligonucleotide containing *S. cerevisiae* DNA.

SEQ ID NO: 14) is a Oligonucleotide containing *A. thaliana* and *S. cerevisiae* DNA.

SEQ ID NO: 15) is an Oligonucleotide containing *S. cerevisiae* DNA.

SEQ ID NO: 16) is an Oligonucleotide containing *S. cerevisiae* DNA.

SEQ ID NO: 17) is Vector pBSNT27 containing *Nicotiana tabacum* DNA.

SEQ ID NO: 18) is an Oligonucleotide containing *N. tabacum* and *S. cerevisiae* DNA.

SEQ ID NO: 19) is an Oligonucleotide containing *N. tabacum* and *A. thaliana* DNA.

SEQ ID NO: 20) is a PCR primer containing *Rhodobacter capsulatus* DNA.

SEQ ID NO: 21) is a PCR is a primer containing *R. capsulatus* DNA.

SEQ ID NO: 22) is a PCR primer containing Schizosaccharomyces pombe DNA.

SEQ ID NO: 23) is a PCR primer containing S. pombe DNA.

SEQ ID NO: 24) is a PCR primer containing *Streptomyces sp* CL190 DNA.

SEQ ID NO: 25) PCR is a primer containing *Streptomyces sp* CL190 DNA.

SEQ ID NO: 26) is an Oligonucleotide containing *S. cerevisiae DNA.*

SEQ ID NO: 27) is an Oligonucleotide *containing S.* cerevisiae DNA.

SEQ ID NO: 28) is an Oligonucleotide containing *Streptomyces sp* CL190 and *R. capsulatus* DNA.

SEQ ID NO: 29) is an Oligonucleotide containing *R. capsulatus* DNA.

SEQ ID NO: 30) is an Oligonucleotide containing *Streptomyces sp* CL190 and *S. cerevisiae* DNA.

SEQ ID NO: 31) is an Oligonucleotide containing *Streptomyces sp* CL190 DNA.

SEQ ID NO: 32) is an Oligonucleotide containing *N. tabacum* and *S. cerevisiae* DNA.

SEQ ID NO: 33) is an Oligonucleotide containing *N. tabacum* and *R. capsulatus* DNA.

SEQ ID NO: 34) is an Oligonucleotide containing *N. tabacum* and *S. cerevisiae* DNA.

SEQ ID NO: 35) is an Oligonucleotide containing *N. tabacum* and *S. pombe* DNA.

SEQ ID NO: 36) is an Oligonucleotide containing NotI restriction site.

SEQ ID NO: 37) is an Oligonucleotide containing NotI restriction site.

SEQ ID NO: 38) is an Oligonucleotide containing *S. cerevisiae* DNA.

SEQ ID NO: 39) is an Oligonucleotide containing *A. thaliana* DNA.

SEQ ID NO: 40) is an Oligonucleotide containing *S. cerevisiae* DNA.

SEQ ID NO: 41) is an Oligonucleotide containing *R. capsulatus* DNA.

SEQ ID NO: 42) is an Oligonucleotide containing *S. cerevisiae* DNA.

SEQ ID NO: 43) is an Oligonucleotide containing *S. pombe* DNA.

SEQ ID NO: 44) is an Oligonucleotide containing *R. capsulatus* DNA.

SEQ ID NO: 45) is an Oligonucleotide containing *R. capsulatus* DNA.

SEQ ID NO: 46) is an Oligonucleotide containing *S. pombe* DNA.

SEQ ID NO: 47) is an Oligonucleotide containing *S. pombe* DNA.

SEQ ID NO: 48) is *Saccharomyces cerevisiae* orf for phosphomevalonate kinase (ERG8).

SEQ ID NO: 49) *Saccharomyces cerevisiae* orf for mevalonate kinase (ERG12).

SEQ ID NO: 50) *Saccharomyces cerevisiae* orf for mevalonate diphosphate decarboxylase (ERG19).

SEQ ID NO: 51) Saccharomyces cerevisiae orf for acetoacetyl thiolase.

SEQ ID NO: 52) *Arabidopsis thaliana* orf for 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) synthase.

SEQ ID NO: 53) *Arabidopsis thaliana* orf for HMG-CoA reductase.

SEQ ID NO: 54) *Schizosaccharomyces pombe* IDI1 (IPP isomerase).

SEQ ID NO: 55) *Rhodobacter* capsulatus idiB (IPP isomerase).

SEQ ID NO: 56) *Streptomyces sp* CL190 orf encoding HMG-CoA reductase.

SEQ ID NO: 57) *Streptomyces sp* CL190 gene cluster containing mevalonate pathway and IPP isomerase orfs.

SEQ ID NO: 58) Operon A containing *A. thaliana* and *S. cerevisiae* DNA

SEQ ID NO: 59) is Operon B containing *A. thaliana* and *S. cerevisiae* DNA.

SEQ ID NO: 60) is Operon C containing *A. thaliana*, *S. cerevisiae*, and *R. capsulatus* DNA.

SEQ ID NO: 61) is Operon D containing *A. thaliana*, *S. cerevisiae*, and *Streptomycs sp* CL190 DNA.

SEQ ID NO: 62) is Operon E containing *A. thaliana*, *S. cerevisiae*, *Streptomycs sp* CL190 DNA, and R. capsulatus DNA.

SEQ ID NO: 63) is Operon F containing containing *S. cerevisiae* and *Streptomycs sp* CL190 DNA.

SEQ ID NO: 64) is Operon G containing *A. thaliana*, *S. cerevisiae* and *S. pombe* DNA.

SEQ ID NO: 65) is PCR primer containing *R. capsulatus* DNA.

SEQ ID NO: 66) is PCR primer containing *R. capsulatus* DNA.

SEQ ID NO: 67) is an Oligonucleotide containing *N. tabacum* and *R. capsulatus* DNA.

SEQ ID NO: 68) is an Oligonucleotide containing *N. tabacum* and *R. capsulatus*

DNA.

SEQ ID NO: 69) is an Oligonucleotide containing *N. tabacum* and *S. cerevisiae* DNA.

SEQ ID NO: 70) is an Oligonucleotide containing *N. tabacum* and *R. capsulatus* DNA.

SEQ ID NO: 71) is *Rhodobacter* capsulatus orf encoding phytoene synthase (crtB).

SEQ ID NO: 72) is plastid transformation vector pHKO4, containing Operon B, containing *A. thaliana* and *S. cerevisiae* DNA.

SEQ ID NO: 73) is plastid transformation vector pHKO7, containing Operon C, containing *A. thaliana, S. cerevisiae,* and *R. capsulatus* DNA.

SEQ ID NO: 74) is plastid transformation vector pHKO8, containing Operon G, containing *A. thaliana, S. cerevisiae,* and *S. pombe* DNA.

SEQ ID NO: 75) is plastid transformation vector pFHO5 containing R. capsulatus DNA encoding phytoene synthase.

SEQ ID NO: 76) is plastid transformation vector pFHO6, containing Operon E, containing *A. thaliana, S. cerevisiae, Streptomycs sp* CL190 DNA, and *R.capsulatus* DNA.

Detailed Description

In the description that follows, a number of terms used in genetic engineering are utilized. In order to provide a clear and consistent understanding of the specification and claims, including the scope to be given such terms, the following definitions are provided.

A protein is considered an isolated protein if it is a protein isolated from a host cell in which it is naturally produced. It can be purified or it can simply be free of other proteins and biological materials with which it is associated in nature, for example, if it is recombinantly produced.

An isolated nucleic acid is a nucleic acid the structure of which is not identical to that of any naturally occurring nucleic acid or to that of any fragment of a naturally occurring genomic nucleic acid spanning more than three separate genes. The term therefore covers, for example, (a) a DNA which has the sequence of part of a naturally

occurring genomic DNA molecule, but is not flanked by both of the coding or noncoding sequences that flank that part of the molecule in the genome of the organism in which it naturally occurs; (b) a nucleic acid incorporated into a vector or into the genomic or plastomic DNA of a prokaryote or eukaryote in a manner such that the resulting molecule is not identical to any naturally occurring vector or genomic or plastomic DNA; (c) a separate molecule such as a cDNA, a genomic or plastomic fragment, a fragment produced by polymerase chain reaction (PCR), or a restriction fragment; and (d) a recombinant nucleotide sequence that is part of a hybrid gene, i.e., a gene encoding a fusion protein. Specifically excluded from this definition are nucleic acids present in mixtures of (i) DNA molecules, (ii) transfected cells, and (iii) cell clones, e.g., as these occur in a DNA library such as a cDNA or genomic DNA library.

One DNA portion or sequence is downstream of second DNA portion or sequence when it is located 3' of the second sequence. One DNA portion or sequence is upstream of a second DNA portion or sequence when it is located 5' of that sequence.

One DNA molecule or sequence and another are heterologous to one another if the two are not derived from the same ultimate natural source, or are not naturally contiguous to each other. The sequences may be natural sequences, or at least one sequence can be derived from two different species or one sequence can be produced by chemical synthesis provided that the nucleotide sequence of the synthesized portion was not derived from the same organism as the other sequence.

A polynucleotide is said to encode a polypeptide if, in its native state or when manipulated by methods known to those skilled in the art, it can be transcribed and/or translated to produce the polypeptide or a fragment thereof. The anti-sense strand of such a polynucleotide is also said to encode the sequence.

A nucleotide sequence is operably linked when it is placed into a functional relationship with another nucleotide sequence. For instance, a promoter is operably linked to a coding sequence if the promoter effects its transcription or expression. Generally, operably linked means that the sequences being linked are contiguous and, where necessary to join two protein coding regions, contiguous and in reading frame. However, it is well known that certain genetic elements, such as enhancers, may be operably linked even at a distance, i.e., even if not contiguous.

In a plastome, sequences are physically linked by virtue of the chromosome

configuration, but they are not necessarily operably linked due to differential expression for example. Transgenes can be physically linked prior to transformation, or can become physically linked once they insert into a plastome. Transgenes can become operably linked if they share regulatory sequences upon insertion into a plastome.

The term recombinant polynucleotide refers to a polynucleotide which is made by the combination of two otherwise separated segments of sequence accomplished by the artificial manipulation of isolated segments of polynucleotides by genetic engineering techniques or by chemical synthesis. In so doing one may join together polynucleotide segments of desired functions to generate a desired combination of functions.

The polynucleotides may also be produced by chemical synthesis, e.g., by the phosphoramidite method described by Beaucage and Caruthers (1981) *Tetra. Letts.*, 22:1859-1862 or the triester method according to Matteuci *et al.* (1981) *J. Am. Chem. Soc.*, 103: 3185, and may be performed on commercial automated oligonucleotide synthesizers. A double-stranded fragment may be obtained from the single stranded product of chemical synthesis either by synthesizing the complementary strand and annealing the strands together under appropriate conditions or by adding the complementary strand using DNA polymerase with an appropriate primer sequence.

Polynucleotide constructs prepared for introduction into a prokaryotic or eukaryotic host will typically, but not always, comprise a replication system (i.e. vector) recognized by the host, including the intended polynucleotide fragment encoding the desired polypeptide, and will preferably, but not necessarily, also include transcription and translational initiation regulatory sequences operably linked to the polypeptide-encoding segment. Expression systems (expression vectors) may include, for example, an origin of replication or autonomously replicating sequence (ARS) and expression control sequences, a promoter, an enhancer and necessary processing information sites, such as ribosome-binding sites, RNA splice sites, polyadenylation sites, transcriptional terminator sequences, and mRNA stabilizing sequences. Signal peptides may also be included where appropriate, preferably from secreted polypeptides of the same or related species, which allow the protein to cross and/or lodge in cell membranes or be secreted from the cell.

Variants or sequences having substantial identity or homology with the polynucleotides encoding enzymes of the mevalonate pathway may be utilized in the

practice of the invention. Such sequences can be referred to as variants or modified sequences. That is, a polynucleotide sequence may be modified yet still retain the ability to encode a polypeptide exhibiting the desired activity. Such variants or modified sequences are thus equivalents. Generally, the variant or modified sequence will comprise at least about 40%-60%, preferably about 60%-80%, more preferably about 80%-90%, and even more preferably about 90%-95% sequence identity with the native sequence.

Sequence relationships between two or more nucleic acids or polynucleotides are generally defined as sequence identity, percentage of sequence identity, and substantial identity. See, for example, "Pedestrian Guide to Analyzing Sequence Data Bases" at www.embl-heidelberg.de/~schneide/paper/springer96/springer.html. In determining sequence identity, a "reference sequence" is used as a basis for sequence comparison. The reference may be a subset or the entirety of a specified sequence. That is, the reference sequence may be a full-length gene sequence or a segment of the gene sequence.

Methods for alignment of sequences for comparison are well known in the art. See, for example, Smith *et al.* (1981) *Adv. Appl. Math.* 2:482; Needleman *et al.* (1970) *J. Mol. Biol.* 48:443; Pearson *et al.* (1988) *Proc. Natl. Acad. Sci.* 85:2444; CLUSTAL in the PC/Gene Program by Intelligenetics, Mountain View, California; GAP, BESTFIT, BLAST, FASTA, and TFASTA in the Wisconsin Genetics Software Package, Genetics Computer Group (GCG), 575 Science Drive, Madison, Wisconsin, USA. Preferred computer alignment methods also include the BLASTP, BLASTN, and BLASTX algorithms. See, Altschul *et al.* (1990) *J. Mol. Biol.* 215:403-410.

"Sequence identity" or "identity" in the context of nucleic acid or polypeptide sequences refers to the nucleic acid bases or residues in the two sequences that are the same when aligned for maximum correspondence over a specified comparison window. "Percentage of sequence identity" refers to the value determined by comparing two optimally aligned sequences over a comparison window, wherein the portion of the polynucleotide sequence in the comparison window may comprise additions or deletions as compared to the reference window for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical nucleic acid base or amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of

positions in the window of comparison, and multiplying the result by 100 to yield the percentage of sequence identity.

Polynucleotide sequences having "substantial identity" are those sequences having at least about 50%-60% sequence identity, generally at least 70% sequence identity, preferably at least 80%, more preferably at least 90%, and most preferably at least 95%, compared to a reference sequence using one of the alignment programs described above. Preferably sequence identity is determined using the default parameters determined by the program. Substantial identity of amino acid sequence generally means sequence identity of at least 50%, more preferably at least 70%, 80%, 90%, and most preferably at least 95%.

Nucleotide sequences are generally substantially identical if the two molecules hybridize to each other under stringent conditions. Generally, stringent conditions are selected to be about 5°C lower than the thermal melting point for the specific sequence at a defined ionic strength and pH. Nucleic acid molecules that do not hybridize to each other under stringent conditions may still be substantially identical if the polypeptides they encode are substantially identical. This may occur, for example, when a copy of a nucleic acid is created using the maximum codon degeneracy permitted by the genetic code.

As noted, hybridization of sequences may be carried out under stringent conditions. By "stringent conditions" is intended conditions under which a probe will hybridize to its target sequence to a detectably greater degree than to other sequences. Stringent conditions are sequence-dependent and will be different in different circumstances. Typically, stringent conditions will be those in which the salt concentration is less than about 1.5 M Na ion, typically about 0.01 to 1.0 M Na ion concentration (or other salts) at pH 7.0 to 8.3 and the temperature is at least about 30° C for short probes (*e.g.*, 10 to 50 nucleotides) and at least about 60° C for long probes (*e.g.*, greater than 50 nucleotides). Stringent conditions may also be achieved with the addition of destabilizing agents such as formamide. Exemplary stringent conditions include hybridization with a buffer solution of 30 to 35% formamide, 1.0 M NaCl, 1% SDS (sodium dodecyl sulphate) at 37◦ C, and a wash in 1X to 2X SSC (20X SSC = 3.0 M NaCl/0.3 M trisodium citrate) at 50 to 55◦ C. It is recognized that the temperature, salt, and wash conditions may be altered to increase or decrease stringency conditions. For

the post-hybridization washes, the critical factors are the ionic strength and temperature of the final wash solution. See, Meinkoth and Wahl (1984) *Anal. Biochem.* 138:267-284.

As indicated, fragments and variants of the nucleotide sequences of the invention are encompassed herein. By "fragment" is intended a portion of the nucleotide sequence. Fragments of the polynucleotide sequence will generally encode polypeptides which retain the biological/enzymatic activity of the native protein. Those of skill in the art routinely generate fragments of polynucleotides of interest through use of commercially available restriction enzymes; synthetic construction of desired polynucleotides based on known sequences; or use of "erase-a-base" technologies such as *Bal* 31 exonuclease, by which the skilled artisan can generate hundreds of fragments of a known polynucleotide sequence from along the entire length of the molecule by time-controlled, limited digestion. Fragments that retain at least one biological or enzymatic activity of the native protein are equivalents of the native protein for that activity.

By "variants" is intended substantially similar sequences. For example, for nucleotide sequences, conservative variants include those sequences that, because of the degeneracy of the genetic code, encode the amino acid sequence of an enzyme of the mevalonate pathway. Variant nucleotide sequences include synthetically derived sequences, such as those generated for example, using site-directed mutagenesis. Generally, nucleotide sequence variants of the invention will have at least 40%, 50%, 60%, 70%, generally 80%, preferably 85%, 90%, up to 95% sequence identity to its respective native nucleotide sequence. Activity of polypeptides encoded by fragments or variants of polynucleotides can be confirmed by assays disclosed herein.

"Variant" in the context of proteins is intended to mean a protein derived from the native protein by deletion or addition of one or more amino acids to the N-terminal and/or C-terminal end of the native protein; deletion or addition of one or more amino acids at one or more sites in the native protein; or substitution of one or more amino acids at one or more sites in the native protein. Such variants may result from, for example, genetic polymorphism or human manipulation. Conservative amino acid substitutions will generally result in variants that retain biological function. Such variants are equivalents of the native protein. Variant proteins that retain a desired biological activity are encompassed within the subject invention. Variant proteins of the invention may include those that are altered in various ways including amino acid substitutions, deletions,

truncations, and insertions. Methods for such manipulation are generally known in the art. See, for example, Kunkel (1985) *Proc. Natl. Acad. Sci. USA* 82:488-492; Kunkel *et al.* (1987) *Methods and Enzymol;*. 154:367-382; and the references cited therein.

An expression cassette may contain at least one polynucleotide of interest to be cotransformed into the organism. Such an expression cassette is preferably provided with a plurality of restriction sites for insertion of the sequences of the invention to be under the transcriptional regulation of the regulatory regions. The expression cassette may additionally contain selectable marker genes.

The cassette may include 5' and 3' regulatory sequences operably linked to a polynucleotide of interest. By "operably linked" is intended, for example, a functional linkage between a promoter and a second sequence, wherein the promoter sequence initiates and mediates transcription of the DNA sequence corresponding to the second sequence. Generally, operably linked means that the nucleic acid sequences being linked are contiguous and, where necessary to join two protein coding regions, contiguous and in the same reading frame. When a polynucleotide comprises a plurality of coding regions that are operably linked such that they are under the control of a single promoter, the polynucleotide may be referred to as an "operon".

The expression cassette will optionally include in the 5'-3' direction of transcription, a transcriptional and translational initiation region, a polynucleotide sequence of interest and a transcriptional and translational termination region functional in plants or microalgae. The transcriptional initiation region, the promoter, is optional, but may be native or analogous, or foreign or heterologous, to the intended host. Additionally, the promoter may be the natural sequence or alternatively a synthetic sequence. By "foreign" is intended that the transcriptional initiation region is not found in the native organism into which the transcriptional initiation region is introduced. As used herein, a chimeric gene comprises a coding sequence operably linked to a transcriptional initiation region that is heterologous to the coding sequence.

The termination region may be native with the transcriptional initiation region, may be native with the operably linked DNA sequence of interest, or may be derived from another source. Convenient termination regions are available from the Ti-plasmid of *A. tumefaciens*, such as the octopine synthase and nopaline synthase termination regions. See also Guerineau *et al.* (1991) *Mol. Gen. Genet.* 262:141-144; Proudfoot

(1991) *Cell* 64:671-674; Sanfacon *et al.* (1991) *Genes Dev.* 5:141-149; Mogen *et al.* (1990) *Plant Cell* 2:1261-1272; Munroe *et al.* (1990) Gene 91:151-158; Ballas *et al.* (1989) *Nucleic Acids Res.* 17:7891-7903; and Joshi *et al.* (1987) *Nucleic Acid Res.* 15:9627-9639.

Where appropriate, the polynucleotides of interest may be optimized for expression in the transformed organism. That is, the genes can be synthesized using plant or algae plastid-preferred codons corresponding to the plastids of the plant or algae of interest. Methods are available in the art for synthesizing such codon optimized polynucleotides. See, for example, U. S. Patent Nos. 5,380,831 and 5,436,391, and Murray *et al.* (1989) *Nucleic Acids Res.* 17:477-498, herein incorporated by reference. Of course, the skilled artisan will appreciate that for the transplastomic purposes described herein, sequence optimization should be conducted with plastid codon usage frequency in mind, rather than the plant or algae genome codon usage exemplified in these references.

It is now well known in the art that when synthesizing a polynucleotide of interest for improved expression in a host cell it is desirable to design the gene such that its frequency of codon usage approaches the frequency of codon usage of the host cell. It is also well known that plastome codon usage may vary from that of the host plant or microalgae genome. For purposes of the subject invention, "frequency of preferred codon usage" refers to the preference exhibited by a specific host cell plastid in usage of nucleotide codons to specify a given amino acid. To determine the frequency of usage of a particular codon in a gene, the number of occurrences of that codon in the gene is divided by the total number of occurrences of all codons specifying the same amino acid in the gene. Similarly, the frequency of preferred codon usage exhibited by a plastid can be calculated by averaging frequency of preferred codon usage in a number of genes expressed by the plastid. It usually is preferable that this analysis be limited to genes that are among those more highly expressed by the plastid. Alternatively, the polynucleotide of interest may be synthesized to have a greater number of the host plastid's most preferred codon for each amino acid, or to reduce the number of codons that are rarely used by the host.

The expression cassettes may additionally contain 5' leader sequences in the expression cassette construct. Such leader sequences can act to enhance translation.

Translation leaders are known in the art and include: picornavirus leaders, for example, EMCV leader (Encephalomyocarditis 5' noncoding region), Elroy-Stein *et al.* (1989) *PNAS USA* 86:6126-6130; potyvirus leaders, for example, TEV leader (Tobacco Etch Virus), Allison *et al.* (1986); MDMV Leader (Maize Dwarf Mosaic Virus) *Virology* 154:9-20; and human immunoglobulin heavy-chain binding protein (BiP), Macejak *et al.* (1991) *Nature* 353:90-94; untranslated leader from the coat protein mRNA of alfalfa mosaic virus (AMV RNA 4), Jobling *et al.* (1987) *Nature* 325:622-625; tobacco mosaic virus leader (TMV), Gallie *et al.* (1989) in *Molecular Biology of RNA*, ed. Cech (Liss, New York), pp. 237-256; and maize chlorotic mottle virus leader (MCMV), Lommel *et al.* (1991) *Virology* 81:382-385. See also, Della-Cioppa *et al.* (1987) *Plant Physiol.* 84:965-968. Other methods known to enhance translation can also be utilized, for example, introns, and the like.

In preparing an expression cassette, the various polynucleotide fragments may be manipulated, so as to provide for the polynucleotide sequences in the proper orientation and, as appropriate, in the proper reading frame. Toward this end, adapters or linkers may be employed to join the polynucleotide fragments or other manipulations may be involved to provide for convenient restriction sites, removal of superfluous nucleotides, removal of restriction sites, or the like. For this purpose, *in vitro* mutagenesis, primer repair, restriction, annealing, resubstitutions, e.g., transitions and transversions, may be involved.

In addition, expressed gene products may be localized to specific organelles in the target cell by ligating DNA or RNA coded for peptide leader sequences to the polynucleotide of interest. Such leader sequences can be obtained from several genes of either plant or other sources. These genes encode cytoplasmically-synthesized proteins directed to, for example, mitochondria (the F1-ATPase beta subunit from yeast or tobacco, cytochrome c1 from yeast), chloroplasts (cytochrome oxidase subunit Va from yeast, small subunit of rubisco from pea), endoplasmic reticulum lumen (protein disulfide isomerase), vacuole (carboxypeptidase Y and proteinase A from yeast, phytohemagglutinin from French bean), peroxisomes (D-aminoacid oxidase, uricase) and lysosomes (hydrolases).

Following transformation, a plant may be regenerated, *e.g.*, from single cells, callus tissue, or leaf discs, as is standard in the art. Almost any plant can be entirely

regenerated from cells, tissues, and organs of the plant. Available techniques are reviewed in Vasil *et al.* (1984) in *Cell Culture and Somatic Cell Genetics of Plants, Vols. I, II, and III, Laboratory Procedures and Their Applications* (Academic press); and Weissbach *et al.* (1989) *Methods for Plant Mol. Biol.*

The transformed plants may then be grown, and either pollinated with the same transformed strain or different strains, and the resulting hybrid having expression of the desired phenotypic characteristic identified. Two or more generations may be grown to ensure that expression of the desired phenotypic characteristic is stably maintained and inherited, and then seeds harvested to ensure expression of the desired phenotypic characteristic has been achieved.

The particular choice of a transformation technology will be determined by its efficiency to transform certain target species, as well as the experience and preference of the person practicing the invention with a particular methodology of choice. It will be apparent to the skilled person that the particular choice of a transformation system to introduce nucleic acid into plant or microalgae plastids is not essential to or a limitation of the invention, nor is the choice of technique for plant regeneration.

Also according to the invention, there is provided a plant or microalgae cell having the constructs of the invention. A further aspect of the present invention provides a method of making such a plant cell involving introduction of a vector including the construct into a plant cell. For integration of the construct into the plastid genome (the "plastome), such introduction will be followed by recombination between the vector and the plastome genome to introduce the operon sequence of nucleotides into the plastome. RNA encoded by the introduced nucleic acid construct (operon) may then be transcribed in the cell and descendants thereof, including cells in plants regenerated from transformed material. A gene stably incorporated into the plastome of a plant or microalgae is passed from generation to generation to descendants of the plant or microalgae, so such descendants should show the desired phenotype.

The present invention also provides a plant or microalgae culture comprising a plant cell as disclosed. Transformed seeds and plant parts are also encompassed. As used herein, the expressions "cell," "cell line," and "cell culture" are used interchangeably and all such designations include progeny, meaning descendants, not limited to the immediate generation of descendants but including all generations of

descendants. Thus, the words "transformants" and "transformed cells" include the primary subject cell and cultures derived therefrom without regard for the number of transfers. It is also understood that all progeny may not be precisely identical in DNA content, due to naturally occurring, deliberate, or inadvertent caused mutations. Mutant progeny that have the same function or biological activity as screened for in the originally transformed cell are included. Where distinct designations are intended, it will be clear from the context.

In addition to a plant or microalgae, the present invention provides any clone of such a plant or microalgae, seed, selfed or hybrid or mated descendants, and any part of any of these, such as cuttings or seed for plants. The invention provides any plant propagule, that is any part which may be used in reproduction or propagation, sexual or asexual, including cuttings, seed, and so on. Also encompassed by the invention is a plant or microalgae which is a sexually or asexually propagated off-spring, clone, or descendant of such a plant or microalgae, or any part or propagule of said plant, off-spring, clone, or descendant. Plant or microalgae extracts and derivatives are also provided.

The present invention may be used for transformation of any plant species, including, but not limited to, corn (*Zea mays*), canola (*Brassica napus, Brassica rapa* ssp.), alfalfa (*Medicago sativa*), rice (*Oryza sativa*), rye (*Secale cereale*), sorghum (*Sorghum bicolor, Sorghum vulgare*), sunflower (*Helianthus annuus*), wheat (*Triticum aestivum*), soybean (*Glycine max*), tobacco (*Nicotiana tabacum*), potato (*Solanum tuberosum*), peanuts (*Arachis hypogaea*), cotton (*Gossypium hirsutum*), sweet potato (*Ipomoea batatus*), cassava (*Manihot esculenta*), coffee (*Cofea* ssp.), coconut (*Cocos nucifera*), pineapple (*Ananas comosus*), citrus trees (*Citrus* spp.), cocoa (*Theobroma cacao*), tea (*Camellia sinensis*), banana (*Musa* spp.), avocado (*Persea americana*), fig (*Ficus casica*), guava (*Psidium guajava*), mango (*Mangifera indica*), olive (*Olea europaea*), papaya (*Carica papaya*), cashew (*Anacardium occidental*), macadamia (*Macadamia integrifolia*), almond (*Prunus amygdalus*), sugar beets (*Beta vulgaris*), oats, barley, vegetables, ornamentals, and conifers.

Preferably, plants of the present invention are crop plants (for example, cereals and pulses, maize, wheat, potatoes, tapioca, rice, sorghum, millet, cassava, barley, pea, and other root, tuber, or seed crops. Important seed crops are oil-seed rape, sugar beet,

maize, sunflower, soybean, and sorghum. Horticultural plants to which the present invention may be applied may include lettuce; endive; and vegetable brassicas including cabbage, broccoli, and cauliflower; and carnations and geraniums. The present invention may be applied to tobacco, cucurbits, carrot, strawberry, sunflower, tomato, pepper, chrysanthemum, petunia, rose, poplar, eucalyptus, and pine.

Grain plants that provide seeds of interest include oil-seed plants and leguminous plants. Seeds of interest include grain seeds, such as corn, wheat, barley, rice, sorghum, rye, etc. Oil seed plants include cotton, soybean, safflower, sunflower, Brassica, maize, alfalfa, palm, coconut, etc. Leguminous plants include beans and peas. Beans including guar, locust bean, fenugreek, soybean, garden beans, cowpea, mungbean, lima bean, fava bean, lentils, chickpea, etc.

Microalgae include but are not limited to the Chlorophyta and the Rhodophyta and may be such organisms as Chlamydomonas, Haematococcus, and Ouneliella.

Other features and advantages of the present invention will become apparent from the following detailed description. It should be understood, however, that the detailed description and the specific examples, while indicating preferred embodiments of the invention, are given by way of illustration only, since various changes and modifications within the spirit and scope of the invention will become apparent to those skilled in the art from this detailed description. Unless indicated otherwise, the respective contents of the documents cited herein are hereby incorporated by reference to the extent they are not inconsistent with the teachings of this specification.

Percentages and ratios given herein are by weight, and temperatures are in degrees Celsius unless otherwise indicated. The references cited within this application are herein incorporated by reference to the extent applicable. Where necessary to better exemplify the invention, percentages and ratios may be cross-combined.

Example 1: Isolation of Orfs Encoding Enzymes of the Mevalonate Pathway for the Construcion of Vectors pFCO1 and pFCO2

In an exemplified embodiment, vectors containing open reading frames (orfs) encoding enzymes of the mevalonate pathway are constructed. Polynucleotides derived from the yeast Saccharomyces cerevisiae, the plant Arabidopsis thaliana, and the eubacterium Streptomyces sp CL190 are used for the construction of vectors, including

plastid delivery vehicles, containing orfs for biosynthesis of the mevalonate pathway enzymes. Construction of the vectors is not limited to the methods described. It is routine for one skilled in the art to choose alternative restriction sites, PCR primers, etc. to create analogous plasmids containing the same orfs or other orfs encoding the enzymes of the mevalonate pathway. Many of the steps in the construction of the plasmids of the subject invention can utilize the joining of blunt-end DNA fragments by ligation. As orientation with respect to the promoter upstream (5') of the described orfs can be critical for biosynthesis of the encoded polypeptides, restriction analysis is used to determine the orientation in all instances involving blunt-end ligations. A novel directional ligation methodology, chain reaction cloning (Pachuk et al., Gene 243:19-25, 2000), can also be used as an alternative to standard ligations in which the resultant orientation of the insert is not fixed. All PCR products are evaluated by sequence analysis as is well known in the art.

The construction of a synthetic operon comprising three yeast orfs encoding phosphomevalonate kinase, mevalonate kinase, and mevalonate diphosphate decarboxylase is described by Hahn et al. (Hahn et al., J. Bacteriol. 183:1-11, 2001). This same synthetic operon, contained within plasmid pFCO2, is able to synthesize, *in vivo*, polypeptides with enzymatic activities able to convert exogenously supplied mevalonate to IPP as demonstrated by the ability of the mevalonate pathway orfs to complement the temperature sensitive dxs::kanr lethal mutation in E. coli strain FH11 (Hahn et al., 2001).

Plasmids pFCO1 and pFCO2 containing a synthetic operon for the biosynthesis of IPP from mevalonate are constructed as follows: Three yeast orfs encoding mevalonate kinase, phosphomevalonate kinase, and mevalonate diphosphate decarboxylase are isolated from S. cerevisiae genomic DNA by PCR using the respective primer sets

FH0129-2:

5' GGACTAGTCTGCAGGAGGAGTTTTAATGTCATTACCGTTCTTAAC TTCTGCACCGGG-3' (sense) (SEQ ID NO: 1) and

FH0129-1:

5' TTCTCGAG*CTTAAGAGTAGCAATATTTACCGGAGCAGTTACACTA*

GCAGTATATACAGTCATTAAAACTCCTCCTGTGAAGTCCATGGTAAATTCG 3' (antisense) (SEQ IDNO:2);

FH0211-1:

5' TAGCGGCCGCAGGAGGAGTTCATATGTCAGAGTTGAGAGCCTTC AGTGCCCCAGGG 3' (sense) (SEQ ID NO: 3) and

FH0211-2:

5' TTTCTGCAGTTTATCAAGATAAGTTTCCGGATCTTT 3' (antisense) (SEQ ID NO: 4);

CT0419-1:

5' GGAATTCATGACCGTTTACACAGCATCCGTTACCGCACCCG 3' (sense) (SEQ ID NO:5) and

CT0419-2:

5' GGCTCGAGTTAAAACTCCTCTTCCTTTGGTAGACCAGTCTTTGCG 3' (antisense) (SEQ ID NO: 6).

Primer FH0129-2 includes a SpeI site (underlined). Primer FH0129-1 contains an XhoI site (underlined), an AflII site (double-underlined), and 54 nucleotides (bold italics) corresponding to the 5' end of the yeast orf for mevalonate diphosphate decarboxylase. Following PCR using primers FH0129-1 and FH0129-2, a product containing the orf encoding yeast mevalonate kinase is isolated by agarose gel electrophoresis and GeneClean purified. Following restriction with SpeI-XhoI, the PCR product is inserted into the SpeI-XhoI sites of pBluescript(SK+) (Stratagene, LaJolla, CA) by ligation to create pBRG12. Primers FH0211-1 and FH0211-2 contain a NotI site (underlined) and a PstI site (underlined), respectively. Following PCR using primers FH0211-1 and FH0211-2, a product containing the orf encoding yeast phosphomevalonate kinase is restricted with NotI-PstI, purified by GeneClean, and inserted into pGEM-T Easy (Promega Corp, Madison, WI) by ligation to create pERG8. An orf encoding yeast mevalonate diphosphate decarboxylase is isolated by PCR using primers CT0419-1 and

CT0419-2 and inserted directly into pGEM-T Easy by ligation to create pERG19. Restriction of pERG8 with NotI-PstI yields a 1.4 Kb DNA fragment containing the orf for phosphomevalonate kinase. Restriction of pBRG12 with NotI-PstI is followed by the insertion of the 1.4 Kb NotI-PstI DNA fragment by ligation to create pBRG812 containing the orfs for both phosphomevalonate kinase and mevalonate kinase and the 5' end of the orf for yeast mevalonate diphosphate decarboxylase. Restriction of pERG19 with AflII-XhoI yields a 1.2 Kb DNA fragment containing the 3' end of the orf for yeast mevalonate diphosphate decarboxylase missing in pBRG812. Insertion of the 1.2 Kb AflII-XhoI DNA fragment into pBRG812/AflII-XhoI by ligation yields pFCO1 containing the three yeast mevalonate pathway orfs (Fig. 1). Restriction of pFCO1 with XhoI is followed by treatment with the Klenow fragment of T7 DNA polymerase and dNTPs to create blunt ends. Subsequent restriction of pFCO1/XhoI/Klenow with SacI yields a 3.9 Kb DNA fragment containing the three yeast mevalonate pathway orfs. Following agarose gel electrophoresis and GeneClean purification of the 3.9 Kb DNA fragment, it is inserted into the SmaI-SacI sites of pNGH1-amp (Garrett et al., J. Biol. Chem. 273:12457-12465, 1998) by ligation to create pFCO2 (Fig. 2).

Example 2: Construction of E. coli strain FH11 (JM101/dxs::kan^r/pDX4)

A mutant E. coli strain containing a disruption of the chromosomal dxs gene is constructed as described by Hamilton et al. (Hamilton et al., J. Bacteriol. 171:4617-4622, 1989). The strains are grown at 30° C or 44° C in Luria-Bertani (LB) supplemented with the following antibiotics as necessary; ampicillin (Amp) (50 (g/ml), chloramphenicol (Cam) (30 (g/ml), and kanamycin (Kan) (25 (g/ml). Within phagemid DD92 (F. R. Blattner, University of Wisconsin, Madison, WI) is a 19.8 Kb EcoRI fragment of E. coli genomic DNA containing dxs, the gene for DXP synthase. Following the isolation of the phage from E. coli strain LE392, DD92 is restricted with SphI, and the resultant 6.3 Kb fragment is isolated by agarose gel electrophoresis. GeneClean purification of the SphI fragment and restriction with SmaI yields a 2.0 Kb SphI-SmaI fragment containing E. coli dxs. The 2.0 Kb fragment is purified by GeneClean and inserted by ligation into the SphI-HindII sites of pMAK705, a plasmid containing a temperature-sensitive origin of replication (Hamilton et al., J. Bacteriol. 171:4617-4622, 1989). The resulting plasmid containing wt dxs, pDX4, is restricted with SapI, a unique site located in the middle of

the dxs gene, and the 5'-overhangs are filled in with Klenow and dNTPs. The blunt-ended DNA fragment is purified by GeneClean and treated with shrimp alkaline phosphatase (SAP, USB Corp., Cleveland, OH) according to the manufacturer's instructions. pUC4K (Amersham Pharmacia Biotech, Piscataway, NJ) is restricted with EcoRI, Klenow-treated, and the resulting 1.3 Kb blunt-ended DNA fragment containing the gene for Kan resistance is inserted into the filled-in SapI site of pDX4 by blunt-end ligation to create pDX5 with a disruption in E. coli dxs. Competent E. coli JM101 cells are transformed with pDX5, a pMAK705 derivative containing dxs::kanr, and grown to an optical density (A600) of 0.6 at 30° C. Approximately 10,000 cells are plated out on LB/Cam medium prewarmed to 44° C. The plates were incubated at 44° C, and several of the resulting colonies are grown at 44° C in 4 ml of LB/Cam medium. Four 50 ml LB/Cam cultures are started with 0.5 ml from four of the 4 ml cultures and grown overnight at 30° C. Four fresh 50 ml LB/Cam cultures are started with 100 µl of the previous cultures and grown overnight at 30° C. An aliquot of one of the 50 ml cultures is serially diluted 5 x 105 fold, and 5 µl is plated on LB/Cam medium. Following incubation at 30° C, the resulting colonies are used to individually inoculate 3 ml of LB medium containing Cam and Kan. Twelve LB/Cam/Kan cultures are grown overnight at 30° C and used for plasmid DNA isolation. *E. coli* cells where the disrupted copy of dxs is incorporated into the genome are identified by restriction analysis of the isolated plasmid DNA and verified by sequence analysis of the DNA contained in the plasmids. The E. coli JM101 derivative containing the dxs::kanr mutation is designated FH11 (Hahn *et al.* 2001).

Example 3: Assay Demonstrating Synthesis of IPP from Mevalonic Acid in E. coli

The episomal copy of dxs contained on pDX4 in E. coli strain FH11 is "turned off" at 44° C due to a temperature sensitive origin of replication on the pMAK705 derivative (Hamilton et al., J. Bacteriol. 171:4617-4622, 1989). The inability of FH11 to grow at the restrictive temperature demonstrates that dxs is an essential single copy gene in E. coli (Hahn et al., 2001). A cassette containing three yeast mevalonate pathway orfs is removed from pFCO1 and inserted into pNGH1-Amp to form pFCO2 for testing the ability of the mevalonate pathway orfs to complement the dxs::kanr disruption when FH11 is grown at 44° C on medium containing mevalonate. The utility of strain FH11

as a component of an assay for testing the ability of mevalonate pathway orfs to direct the synthesis of IPP is demonstrated as follows:

Colonies of E. coli strain FH11 transformed with pFCO2 or pNGH1-Amp, the expression vector without an insert, are isolated by incubation at 30° C on LB plates containing Kan and Amp. Four ml LB/Kan/Amp cultures containing either FH11/pFCO2 or FH11/pNGH1-Amp are grown overnight at 30° C. Following a 10,000-fold dilution, 10 µl portions from the cultures are spread on LB/Kan/Amp plates that are prewarmed to 44° C or are at rt. Approximately 1.3 mg of mevalonic acid is spread on each plate used for FH11/pFCO2. The prewarmed plates are incubated at 44° C, and the rt plates are incubated at 30° C overnight.

FH11/pNGH1-amp cells will not grow at the restrictive temperature of 44° C and FH11/pFCO2 cells are unable to grow at of 44° C unless mevalonic acid (50 mg/L) is added to the growth medium thus establishing the ability of the polypeptides encoded by the mevalonate pathway orfs contained in the synthetic operon within pFCO2 to form IPP from mevalonate in vivo (Hahn *et al.*, 2001).

Example 4: Isolation of Mevalonate Pathway Orfs

In a specific, exemplified embodiment, the isolation of orfs, each encoding a polypeptide with either HMG-CoA synthase enzyme activity, HMG-CoA reductase enzyme activity, or acetoacetyl-CoA thiolase enzyme activity, and construction of vectors containing these orfs is as follows: Synthesis of A. thaliana first strand cDNAs is performed utilizing PowerScript™(reverse transcriptase (Clontech Laboratories, Inc., Palo Alto, CA) according to the manufacturer's instructions. Specifically, a microfuge tube containing 5 µl of A. thaliana RNA (Arabidopsis Biological Resource Center, Ohio State University, Columbus, OH), 1.8 µl poly(dT)15 primer (0.28 µg/µl, Integrated DNA Technologies, Inc.. Coralville, IA), and 6.2 µl DEPC-treated H2O is heated at 70°C for 10 min and then immediately cooled on ice. The mixture is spun down by centrifugation and 4 µl of 5X First-Strand Buffer (Clontech), 2 µ(l Advantage UltraPure PCR dNTP mix (10 mM each, Clontech) and 2 µ(l 100 mM DTT are added and the entire contents mixed by pipetting. Following the addition of 1 µ(l reverse transcriptase (Clontech) and mixing by pipetting, the contents are incubated at 42° C for 90 min and then heated at 70° C for 15 min to terminate the reaction.

The resulting *A. thaliana* first strand cDNAs are used as templates for the synthesis of an orf encoding HMG-CoA synthase and a truncated HMG-CoA reductase by PCR in a Perkin-Elmer GeneAmp PCR System 2400 thermal cycler utilizing the Advantage®-HF 2 PCR Kit (Clontech) according to the manufacturer's instructions. An *A. thaliana* HMG-CoA synthase orf is isolated using the following PCR primers:

1) 5' GCTCTAGATGCGCAGGAGGCACATATGGCGAAGAACGTTGGGATTTTG GCTATGGATATCTATTTCCC 3' (sense) (SEQ ID NO: 7); and

2) 5' CG***CTCGAG***TCGACGGATCCTCAGTGTCCATTGGCTACAGATCCATCTTC ACCTTTCTTGCC 3' (antisense) (SEQ ID NO: 8);

containing the restriction site *Xba*I shown underlined, the restriction site *Xho*I shown in bold italic and the restriction site *Sal*I shown double underlined. Specifically, 2 (l cDNA, 5 μ(l 10X HF 2 PCR Buffer (Clontech), 5 μl 10X HF 2 dNTP Mix (Clontech), 1 μl each of the primers described above, 1 μl 50X Advantage-HF 2 Polymerase Mix (Clontech), and 35 μl PCR-Grade H2O (Clontech) are combined in a 0.5 ml PCR tube. The mixture is heated at 94° C for 15 sec then subjected to 40 PCR cycles consisting of 15 sec at 94° C and 4 min at 68° C. After a final incubation at 68° C for 3 min, the reaction is cooled to 4° C. Agarose gel electrophoresis is performed on a 10 μl aliquot to confirm the presence of a DNA fragment of the predicted size of 1.4 Kb. The PCR is repeated in triplicate to generate enough product for its isolation by gel excision and purification by GeneClean (Qbiogene, Inc., Carlsbad CA). Following restriction with *Xba*I-*Xho*I and purification by GeneClean, the 1.4 Kb PCR product is inserted into the *Xba*I-*Xho*I sites of pBluescript(SK+) by ligation to form putative pBSHMGS constructs. Sequence analysis of several of the candidate constructs is performed to identify inserts with DNA identical to the published *A. thaliana* orf for HMG-CoA synthase and are used for the construction of pBSHMGSR as described below.

An *A. thaliana* orf encoding a polypeptide with HMG-CoA reductase enzyme activity is synthesized by PCR essentially as described above using the following primers:

3) 5' CCGCTCGAGCACGTGGAGGCACATATGCAATGCTGTGAGATGCCT GTTGGATACATTCAGATTCCTGTTGGG 3' (sense) (SEQ ID NO: 9); and

4) 5' GG*GGTACC*TG**CGGCCG**GATCCCGGGTCATGTTGTTGTTGTTGTCGT TGTCGTTGCTCCAGAGATGTCTCGG 3' (antisense) (SEQ ID NO: 10);

containing the restriction site *Xho*I shown underlined, the restriction site *Kpn*I shown in italic, the restriction site *Eag*I shown in bold, and the restriction site *Sma*I shown double underlined. The 1.1 Kb PCR product is isolated by agarose gel electrophoresis, purified by GeneClean and inserted into the pT7Blue-3 vector (Novagen, Inc., Madison, WI) using the Perfectly Blunt™ Cloning Kit (Novagen) according to the manufacturer's instructions. Sequence analysis is performed to identify constructs containing *A. thaliana* DNA encoding the desired C-terminal portion of the published HMG-CoA reductase amino acid sequence and are designated pHMGR.

PCR is performed on *S. cerevisiae* genomic DNA (Invitrogen, Corp., Carlsbad, CA) by using the Advantage®-HF 2 PCR Kit (Clontech) according to the manufacturer's instructions and the following primers:

5) 5' ACAACA*CCGCGGC*GGCCGC**GTCGAC**TACGTAGGAGGCACATATGTC TCAGAACGTTTACATTGTATCGACTGCC 3' (sense) (SEQ ID NO: 11); and

6) 5' GC***TCTAGA***GGATCCTCATATCTTTTCAATGACAATAGAGGAAGCACC ACCACC 3' (antisense) (SEQ ID NO: 12);

containing the restriction site *Not*I shown underlined, the restriction site *Sac*II shown in italic, the restriction site *Sal*I shown in bold, the restriction site SnaBI shown double underlined, and the restriction site *Xba*I in bold italic. The 1.2 Kb PCR product is isolated by agarose gel electrophoresis, purified by GeneClean and inserted into the vector pT7Blue-3 (Novagen,) using the Perfectly Blunt™ Cloning Kit (Novagen) according to the manufacturer's instructions. Sequence analysis is performed to identify constructs containing *S. cerevisiae* DNA identical to the published orf encoding acetoacetyl-CoA thiolase and they are designated pAACT.

Example 5: Construction of pHKO1

In an exemplified embodiment, a pBluescript(SK+) derivative containing an operon with orfs encoding polypeptides with enzymatic activities for HMG-CoA synthase, HMG-CoA reductase, and acetoacetyl-CoA thiolase is constructed as follows: Following restriction of pHMGR with *Xho*I-*Kpn*I, isolation of the 1.1 Kb DNA fragment by agarose gel electrophoresis, and purification by GeneClean, the 1.1 Kb *Xho*I-*Kpn*I DNA fragment containing the orf encoding the C-terminal portion of *A. thaliana* HMG-CoA reductase is inserted into the *Sal*I-*Kpn*I sites of pBSHMGS by ligation to

create pBSHMGSR. Following restriction of pAACT with *Sac*II-*Xba*I, isolation of the 1.2 Kb DNA fragment containing the orf encoding yeast acetoacetyl-CoA thiolase by agarose gel electrophoresis, and purification by GeneClean, the 1.2 Kb *Sac*II-*Xba*I DNA fragment is inserted into the *Sac*II-*Xba*I sites of pBSHMGSR by ligation to create pHKO1 (Fig. 3).

Example 6: Construction of pHKO2

In a specific, exemplified embodiment, a vector containing a synthetic operon consisting of six orfs encoding polypeptides with acetoacetyl-CoA thiolase, HMG-CoA synthase, HMG-CoA reductase, mevalonate kinase, phosphomevalonate kinase, and mevalonate diphosphate decarboxylase enzymatic activities, thus comprising the entire mevalonate pathway, is constructed as follows: Restriction of pHKO1 with *Eag*I yields a 3.7 Kb DNA fragment containing orfs encoding yeast acetoacetyl-CoA thiolase, *A. thaliana* HMG-CoA synthase, and a truncated *A. thaliana* HMG-CoA reductase. Following isolation of the 3.7 Kb *Eag*I DNA fragment by agarose gel electrophoresis and purification by GeneClean, it is directionally inserted into the *Not*I site of pFCO2 (Hahn *et al.*, 2001) utilizing the methodology of chain reaction cloning (Pachuk et al., 2000), thermostable Ampligase((Epicentre Technologies, Madison, WI), and the following bridge oligonucleotide primers:

1) 5' TGGAATTCGAGCTCCACCGCGGTGGCGGCCGCGTCGACGCCGGCGGAG GCACATATGTCT 3'(SEQ ID NO: 13); and

2) 5' AACAACAACAACATGACCCGGGATCCGGCCGCAGGAGGAGTTCATATG TCAGAGTTGAGA 3'(SEQ ID NO: 14);

as follows: Agarose gel electrophoresis is performed on the 8.1 Kb pFCO2/*Not*I DNA fragment and the 3.7 Kb *Eag*I DNA fragment isolated from pHKO1 to visually estimate their relative concentrations. Approximately equivalent amounts of each fragment totaling 4.5 µl, 1 µl of each bridge oligo at a concentration of 200 nM, 5 µl Ampligase® 10X Reaction Buffer (Epicentre), 3 µl Ampligase® (5U/(l) (Epicentre), and 35.5 µl PCR grade H2O are added to a 0.5 ml PCR tube. The mixture is heated at 94° C for 2 min then subjected to 50 PCR cycles consisting of 30 sec at 94° C, 30 sec at 60° C, and 1 min at 66° C. After a final incubation at 66° C for 5 min, the reaction is cooled to 4° C. Colonies resulting from the transformation of *E. coli* strain NovaBlue (Novagen) with 1

μl of the directional ligation reaction are grown in LB medium supplemented with ampicillin at a final concentration of 50 μg/ml. Restriction analysis with NaeI-KpnI of mini-prep plasmid DNA from the liquid cultures is performed to identify candidate pHKO2 constructs by the presence of both a 5.7 and a 6.2 Kb DNA fragment. Further analysis by restriction with *Sma*I-*Xho*I to generate both a 3.9 and 7.9 Kb DNA fragment confirms the successful construction of pHKO2 (Fig. 4).

Example 7:Assay Demonstrating the Synthesis of IPP from Acetyl-CoA in E. coli

In a specific, exemplified embodiment, a derivative of pNGH1-amp (Hahn *et al.*, 2001), containing the entire mevalonate pathway, is assayed (Fig. 5) for its ability to synthesize IPP from endogenous acetyl-CoA in *E. coli* strain FH11, containing the temperature sensitive *dxs*::kan^r knockout (Hahn *et al.*, 2001), as follows: Colonies resulting from the transformation of FH11, by pHKO2, containing orfs encoding polypeptides with enzymatic activities for acetoacetyl-CoA thiolase, HMG-CoA synthase, HMG-CoA reductase, mevalonate kinase, phosphomevalonate kinase, and mevalonate diphosphate decarboxylase, are isolated by incubation at 30° C on LB plates containing Kan and Amp. Several 4 ml LB/Kan/amp samples are individually inoculated with single colonies from the FH11/pHKO2 transformation. Following growth at 30° C overnight, the FH11/pHKO2 cultures are diluted 100,000-fold, and 5 μl aliquots are spread on LB/Kan/amp plates at room temperature (rt) or that are prewarmed to 44° C. The prewarmed plates are incubated at 44° C, and the rt plates are incubated at 30° C overnight. FH11 and FH11/pNGH1amp cells will not grow at the restrictive temperature of 44° C (Hahn *et al.*, 2001). FH11/pHKO2 cells are able to grow at 44° C, thus establishing the ability, of a synthetic operon comprising the entire mevalonate pathway, to form IPP from acetyl-CoA and thereby overcome the dxs::kan^r block to MEP pathway biosynthesis of IPP in *E. coli* strain FH11.

Example 8: Construction of pHKO3

In another exemplified embodiment, a derivative of pBluescript(SK+) containing an operon comprising orfs, which in their summation is the entire mevalonate pathway, is constructed as follows: pHKO1, containing orfs encoding acetoacetyl-CoA thiolase, HMG-CoA synthase, and an N-terminal truncated HMG-CoA reductase, is restricted with

*Sal*I-*Not*I and purified by GeneClean. The pBluescript(SK+) derivative pFCO1, containing the orfs encoding mevalonate kinase, phosphomevalonate kinase, and mevalonate diphosphate decarboxylase, has been described above in Example 1. Following restriction of pFCO1 with *Xho*I-*Not*I, isolation by agarose gel electrophoresis, and purification by GeneClean, the 3.9 Kb DNA fragment containing the mevalonate pathway orfs is inserted into pHKO1/*Sal*I-*Not*I by directional ligation (Pachuk *et al.*, 2000) utilizing thermostable Ampligase® (Epicentre Technologies, Madison, WI), and the following bridging oligonucleotides:

1) 5' CTCAACTCTGACATATGAACTCCTCCTGCGGCCGCCGCGGTGGAGCTCC AGCTTTTGTTCCC 3' (SEQ ID NO: 15); and

2) 5' GGTCTACCAAAGGAAGAGGAGTTTTAACTCGACGCCGGCGGAGGCACA TATGTCTCAGAACG 3' (SEQ ID NO: 16);

essentially as described for the construction of pHKO2. Restriction analysis is performed with KpnI to confirm the successful construction of pHKO3 (Fig. 6).

Example 9: Construction of Tobacco Plastid Transformation Vector pHKO4

In an exemplified embodiment, a vector containing a *Nicotiana tabacum* plastid pseudogene is utilized to create a plastid transformation vector as follows: The pBluescript(SK+) derivative designated as pBSNT27 (Fig. 7, SEQ ID NO: 17) contains a 3.3 Kb *Bgl*II-*Bam*HI DNA fragment of the *N. tabacum* chloroplast genome corresponding approximately to base-pairs 80553-83810 of the published nucleotide sequence (Sugiura, M., 1986, and Tsudsuki, T., 1998.). A unique restriction site contained within the tobacco *inf*A pseudogene located on pBSNT27 is cleaved with *Bgl*II and the resulting 5' overhangs are filled in with Klenow and dNTPs. The resulting 6.2 Kb blunt-ended DNA fragment is GeneClean purified. Following restriction of pHKO3 with *Eag*I, filling in of the resulting 5' overhangs with Klenow and dNTPs, isolation by agarose gel electrophoresis, and purification by GeneClean, the resulting 7.7 Kb blunt-ended DNA fragment, containing orfs encoding the entire mevalonate pathway, is directionally inserted into the blunt-ended BglII site of pBSNT27 utilizing chain reaction cloning (Pachuk *et al.*, 2000.), thermostable Ampligase® (Epicentre Technologies, Madison, WI), and the following bridging oligonucleotides:

1) 5' GATCTTTCCTGAAACATAATTTATAATCAGATCGGCCGCAGGAGGAG

TTCATATGTCAGAGTTGAG 3' (SEQ ID NO: 18); and

2) GACAACAACAACAACATGACCCGGGATCCGGCCGATCTAAACAAACCCG GAACAGACCGTTGGGAA 3' (SEQ ID NO: 19);

to form the tobacco plastid-specific transformation vector pHKO4 (Fig. 8).

Alternatively, other derivatives of pBSNT27 can be constructed, using skills as known in the art, that are not reliant upon an available restriction site(s) in the pseudogene. For example, although the infA pseudogene comprises basepairs 3861-4150 in pBSNT27, there are unique restriction sites in close proximity, upsteam and downstream, that can be utilized to excise the entire pseudogene followed by its replacement with an orf or gene cluster comprising multiple orfs, e.g. the complete mevalonate pathway described above. Specifically, there is a unique BsrGI site at 3708 base pairs and a unique SexAI restriction site at 4433 base pairs within pBSNT27. Thus, as will be readily apparent to those skilled in the art, one can replace the infA pseudogene entirely by inserting a BsrGI- SexAI DNA fragment containing DNA, comprising orfs encoding the entire mevalonate pathway, that is flanked by the excised DNA originally flanking the infA pseudogene, i.e. DNA corresponding to 3708-3860 and 4151-4433 base pairs in pBSNT27. The resultant construct will be missing the pseudogene, but will contain the excised flanking DNA restored to its original position and now surrounding the mevalonate pathway orfs. Also, a similar strategy, that will also be apparent to those skilled in the art in view of this disclosure, can be employed that restores the intact pseudogene to a location between the DNA originally flanking it, yet linked to an orf or orfs located upstream and/or downstream of the pseudogene and adjacent to the original flanking DNA.

Example 10: Construction of Vectors Containing Orfs Encoding IPP Isomerase (pHKO5 and pHKO6)

In a specific, exemplified embodiment, orfs encoding IPP isomerase are isolated and vectors containing an operon comprising orfs for the entire mevalonate pathway and an additional orf for IPP isomerase are constructed as follows: A *Rhodobacter capsulatus* orf encoding a polypeptide with IPP isomerase activity is isolated by PCR from genomic DNA (J. E. Hearst, Lawrence Berkeley Laboratories, Berkeley, CA) using the following primers:

1) 5' CGCTCGAG**TACGTA**AGGAGGCACATATGAGTGAGCTTATACCCGCCTG GGTTGG 3' (sense) (SEQ ID NO: 20); and

2) 5' GC*TCTAGA*GATATCGGATCC**GCGGCCG**CTCAGCCGCGCAGGATCGATCC GAAAATCC 3' (antisense) (SEQ ID NO: 21);

containing the restriction sites *Xho*I shown underlined, *Bsa*AI shown in bold, *Xba*I shown in italic, *Eco*RV shown double underlined, and *Not*I shown in bold italic. The PCR product is restricted with *Xho*I-*Xba*I, isolated by agarose gel electrophoresis, purified by GeneClean, and inserted into the *Xho*I-*Xba*I sites of pBluescript(SK+) by ligation to form pBSIDI. Sequence analysis is performed to identify the plasmids containing *R. capsulatus* DNA identical to the complementary sequence of base pairs 34678-34148, located on contig rc04 (Rhodobacter Capsulapedia, University of Chicago, Chicago, IL). Following restriction of pBSIDI with *Bsa*AI-*Eco*RV, agarose gel electrophoresis and GeneClean purification, the 0.5 Kb *Bsa*AI-*Eco*RV DNA fragment containing the *R. capsulatus* orf is inserted into the dephosphorylated *Sma*I site of pHKO3 by blunt-end ligation to create pHKO5 (Fig. 9). This establishes the isolation of a previously unknown and unique orf encoding *R. capsulatus* IPP isomerase.

A *Schizosaccharomyces pombe* orf encoding a polypeptide with IPP isomerase activity is isolated from plasmid pBSF19 (Hahn and Poulter, J. Biol. Chem. 270:11298-11303, 1995) by PCR using the following primers

3) 5' GCTCTAGA**TACGTA**GGAGGCACATATGAGTTCCCAACAAGAGAAAAA GGATTATGATGAAGAACAATTAAGG 3' (sense) (SEQ ID NO: 22); and

4) 5' CGCTCGAGCCCGGGGGATCCTTAGCAACGATGAATTAAGGTATCTTGG AATTTTGACGC 3' (antisense) (SEQ ID NO: 23);

containing the restriction site *Bsa*AI shown in bold and the restriction site *Sma*I shown double underlined. The 0.7 Kb PCR product is isolated by agarose gel electrophoresis, purified by GeneClean and inserted into the pT7Blue-3 vector (Novagen, Inc., Madison, WI) using the Perfectly Blunt™ Cloning Kit (Novagen) according to the manufacturer's instructions. Sequence analysis is performed to identify constructs containing *S. pombe* DNA identical to the published DNA sequence (Hahn and Poulter, 1995) and are designated pIDI. Following restriction of pIDI with *Bsa*AI-*Sma*I, isolation by agarose gel electrophoresis, and purification by GeneClean, the 0.7 Kb *Bsa*AI-*Sma*I DNA fragment containing the orf encoding *S. pombe* IPP isomerase is inserted into the dephosphorylated

*Sma*I site of pHKO3 by blunt-end ligation to create pHKO6.

Example 11: Construction of Vectors Containing Alternative Orfs for Mevalonate Pathway Enzymes and IPP Isomerase

In another exemplified embodiment, vectors containing open reading frames (orfs) encoding enzymes of the mevalonate pathway and IPP isomerase other than those described above are constructed. Polynucleotides derived from the yeast *Saccharomyces cerevisiae*, the plant *Arabidopsis thaliana*, and the bacteria *Rhodobacter capsulatus* and Streptomyces sp strain CL190 are used for the construction of vectors, including plastid delivery vehicles, containing orfs for biosynthesis of the encoded enzymes. Construction of the vectors is not limited to the methods described. One skilled in the art may choose alternative restriction sites, PCR primers, etc. to create analogous plasmids containing the same orfs or other orfs encoding the enzymes of the mevalonate pathway and IPP isomerase.

Specifically, by way of example, genomic DNA is isolated from Streptomyces sp strain CL190 (American Type Culture Collection, Manassas, VA) using the DNeasy Tissue Kit (Qiagen) according to the manufacturer's instructions. An orf encoding a polypeptide with HMG-CoA reductase activity (Takahashi *et al.*, J. Bacteriol. 181:1256-1263, 1999) is isolated from the Streptomyces DNA by PCR using the following primers :

1) 5' CCGCTCGAGCACGTGAGGAGGCACATATGACGGAAACGCACGCCATAG CCGGGGTCCCGATGAGG 3' (sense) (SEQ ID NO: 24); and

2) 5' GG*GGTACC***GCGGCCGC**ACGCGTCTATGCACCAACCTTTGCGGTCTT GTTGTCGCGTTCCAGCTGG 3' (antisense) (SEQ ID NO: 25);

containing the restriction site *Xho*I shown underlined, the restriction site *Kpn*I shown in italics, the restriction site *Not*I shown in bold, and the restriction site *Mlu*I shown double underlined. The 1.1 Kb PCR product is isolated by agarose gel electrophoresis, purified by GeneClean and inserted into the pT7Blue-3 vector (Novagen, Inc., Madison, WI) using the Perfectly Blunt™ Cloning Kit (Novagen) according to the manufacturer's instructions. Sequence analysis is performed to identify constructs containing Streptomyces sp CL190 DNA identical to the published sequence and are designated pHMGR2.

Alternatively, using skills as known in the art, an orf encoding a truncated *S. cerevisiae* HMG-CoA reductase (Chappel et al., US patent 5,349,126 1994) can be isolated by PCR and inserted into pT7Blue-3 (Novagen, Inc., Madison, WI) to construct a vector for use in building a gene cluster comprising the entire mevalonate pathway, in an analgous fashion to the use of the Streptomyces sp CL190 orf encoding HMG-CoA reductase, as described herein.

Following restriction of pAACT (see Example 4) with *Sac*II-*Xba*I, isolation of the 1.2 Kb DNA fragment containing the orf encoding yeast acetoacetyl-CoA thiolase by agarose gel electrophoresis, and purification by GeneClean, the 1.2 Kb *Sac*II-*Xba*I DNA fragment is inserted into the *Sac*II-*Xba*I sites of pBSHMGS (see Example 4) by ligation to create pBSCTGS. Following restriction of pHMGR2 with *Xho*I-*Kpn*I, isolation of the 1.1 Kb DNA fragment by agarose gel electrophoresis, and purification by GeneClean, the 1.1 Kb *Xho*I-*Kpn*I DNA fragment containing the orf encoding *Streptomyces* sp CL190 HMG-CoA reductase is inserted into the *Xho*I-*Kpn*I sites of pBSCTGS by ligation to create the pBluescript(SK+) derivative, pFHO1 (Fig. 10).

A derivative of pFHO1 containing an operon with orfs, which in their summation comprise the entire mevalonate pathway, is constructed as follows: pFHO1 is restricted with *Sna*BI and the resulting 6.6 Kb blunt-ended DNA fragment is purified by GeneClean. Following the restriction of pFCO1 (see Example 1) with *Not*I-*Xho*I, the resulting 3.9 Kb DNA fragment is isolated by agarose gel electrophoresis and purified by GeneClean. The 5' overhangs of the 3.9 Kb DNA fragment are filled in with Klenow and dNTPs. Following purification by GeneClean, the blunt-ended DNA fragment containing three mevalonate pathway orfs (Hahn *et al.*, 2001) is inserted into the *Sna*BI site of pFHO1 utilizing directional ligation methodology (Pachuk *et al.*, 2000), thermostable Ampligase® (Epicentre Technologies, Madison, WI), and the bridging oligonucleotides:

3) 5' GAGCTCCACCGCGGCGGCCGCGTCGACTACGGCCGCAGGAGGAGTTCA TATGTCAGAGTT 3' (SEQ ID NO: 26); and

4) 5' TCTACCAAAGGAAGAGGAGTTTTAACTCGAGTAGGAGGCACATATGTC TCAGAACGTTTA 3' (SEQ ID NO: 27);

to form pFHO2 (Fig. 11).

A derivative of pFHO2 containing an operon with orfs, which in their summation comprise the entire mevalonate pathway and an orf encoding IPP isomerase is constructed

as follows: pFHO2 is restricted with *Mlu*I and the resulting 5' overhangs are filled in with Klenow and dNTPs. The 10.6 Kb blunt-ended DNA fragment is purified by GeneClean. Following restriction of pBSIDI with *Bsa*AI-*Eco*RV, agarose gel electrophoresis and GeneClean purification, the resulting blunt-ended 0.5 Kb DNA fragment containing the *R. capsulatus* IPP isomerase orf is inserted into the filled in *Mlu*I site of pFHO2 utilizing directional ligation methodology (Pachuk *et al.*, 2000), thermostable Ampligase® (Epicentre Technologies, Madison, WI), and the following bridging oligonucleotides:

5) 5' CAAGACCGCAAAGGTTGGTGCATAGACGCGGTAAGGAGGCACATATGA GTGAGCTTATAC 3' (SEQ ID NO: 28); and

6) 5' CCTGCGCGGCTGAGCGGCCGCGGATCCGATCGCGTGCGGCCGCGGTACC CAATTCGCCCT 3'(SEQ ID NO: 29);

to form pFHO3 (Fig. 12).

Following the restriction of pBluescript(SK+) with SacII-*Xba*I and purification by GeneClean, a 1.3 Kb *Sac*II-*Xba*I DNA fragment containing the orf encoding *S. cerevisiae* acetoacetyl-CoA thiolase, isolated from pAACT (see Example 4) by restriction and agarose gel electrophoresis, is inserted into pBluescript(SK+)/*Sac*II-*Xba*I by ligation. The resulting plasmid, pBSAACT, is restricted with *Xba*I, treated with Klenow and dNTPs, and purified by GeneClean. Following restriction of *Streptomyces* sp CL190 genomic DNA with *Sna*BI, a blunt-ended 6.8 Kb DNA fragment, containing five (5) orfs encoding polypeptides with HMG-CoA synthase, HMG-CoA reductase, mevalonate kinase, phosphomevalonate kinase, mevalonate diphosphate decarboxylase and IPP isomerase enzymatic activities (Takagi *et al.*, J. Bacteriol. 182:4153-4157, 2000 and Kuzuyama *et al.*, Proc. Natl. Acad. Sci. USA 98:932-7, 2001), is isolated by agarose gel electrophoresis, purified by GeneClean and inserted into the filled in *Xba*I site of pBSAACT utilizing directional ligation methodology (Pachuk *et al.*, 2000), thermostable Ampligase® (Epicentre Technologies, Madison, WI), and the bridging oligonucleotides:

7) 5' TGTCATTGAAAAGATATGAGGATCCTCTAGGTACTTCCCTGGCGTGTGC AGCGGTTGACG 3' (SEQ ID NO: 30); and

8) 5' CGATTCCGCATTATCGGTACGGGTGCCTACCTAGAACTAGTGGATCCCC CGGGCTGCAGG 3' (SEQ ID NO: 31);

to form pFHO4 (Fig 13). Transformation experiments to isolate pFHO4 constructs are performed with *E. coli* competent cells utilizing media containing ampicillin.

Alternatively, media containing only fosmidomycin (20 μg/ml) as the selection agent is used for the direct isolation of pFHO4 constructs containing the *Streptomyces* sp CL190 gene cluster.

The construction of vectors pHKO2, pHKO3, pHKO5, pHKO6, pFHO2, pFHO3, and pFHO4, illustrates the many ways of combining orfs isolated from a variety of organisms to encode polypeptides such that in their summation they comprise the entire mevalonate pathway or comprise the entire mevalonate pathway and IPP isomerase.

Example 12: Construction of Tobacco Plastid Transformation Vectors pHKO7 and pHKO8

In a specific, exemplified embodiment, tobacco plastid-specific transformation vectors containing orfs, which in their summation comprise the mevalonate pathway, and an additional orf encoding IPP isomerase are constructed as follows: Restriction of pHKO5 with *Not*I generates a DNA fragment containing six orfs comprising the entire mevalonate pathway and an additional orf encoding *R. capsulatus* IPP isomerase. Restriction of pHKO6 with *Eag*I generates a DNA fragment containing the six orfs comprising the complete mevalonate pathway and an additional orf encoding *S. pombe* IPP isomerase. Following isolation by agarose gel electrophoresis and purification by GeneClean, the 8.2 Kb NotI DNA fragment from pHKO5 is blunt-ended with Klenow and dNTPs and inserted into the blunt-ended *Bgl*II site of pBSNT27 utilizing chain reaction cloning (Pachuk *et al.*, 2000), thermostable Ampligase® (Epicentre Technologies, Madison, WI), and the following bridging oligonucleotides:

1) 5' CTTTCCTGAAACATAATTTATAATCAGATCGGCCGCAGGAGGAGTTCA TATGTCAGAGTT 3' (SEQ ID NO: 32); and

2) 5'TTCGGATCGATCCTGCGCGGCTGAGCGGCCGATCTAAACAAACCCGGA ACAGACCGTTGG 3' (SEQ ID NO: 33);

to create the plastid delivery vehicle pHKO7 (Fig. 14) containing orfs encoding the entire mevalonate pathway and an orf encoding *R. capsulatus* IPP isomerase. Following isolation by agarose gel electrophoresis and purification by GeneClean, the 8.4 Kb *Eag*I DNA fragment from pHKO6 is blunt-ended with Klenow and dNTPs and inserted into the blunt-ended *Bgl*II site of pBSNT27 utilizing chain reaction cloning (Pachuk *et al.*, 2000), thermostable Ampligase® (Epicentre Technologies, Madison, WI), and the

following bridging oligonucleotides:

3) 5' CTTTCCTGAAACATAATTTATAATCAGATCGGCCGCAGGAGGAGTTCA TATGTCAGAGT 3' (SEQ ID NO: 34); and

4) 5' TCGTTGCTAAGGATCCCCCGGGATCCGGCCGATCTAAACAAACCCGGA ACAGACCGTTGG 3' (SEQ ID NO: 35);

to create the plastid delivery vehicle pHKO8 containing orfs encoding the entire mevalonate pathway plus the *S. pombe* IPP isomerase orf.

Alternatively, either of the IPP isomerase orfs described above can be solely inserted, without orfs for the mevalonate pathway, directly into pBSNT27 (or into any suitable plant transformation vector, known in the art), using skills known in the art.

Example 13: Construction of Vectors used for Increasing Carotenoid Production (pHKO9, pHK10, pHK11, pHK12, and pHK13)

In yet another exemplified embodiment, a derivative of pTrcHisB (Invitrogen) containing a synthetic operon comprising orfs, which in their summation is the entire mevalonate pathway, is constructed as follows: A unique *Not*I site was inserted into pTrcHisB utilizing the following oligonucleotides:

1) 5' CATGGCGGCCGCG 3' (SEQ ID NO: 36); and

2) 5' GATCCGCGGCCGC 3' (SEQ ID NO: 37);

that upon annealing, form a double-stranded DNA linker containing *Not*I with 5' overhangs compatible with *Sty*I and *Bam*HI. Following restriction of pTrcHisB with *Sty*I-*Bam*HI, isolation of the resulting 4.3 Kb DNA fragment by agarose gel electrophoresis, and its purification by GeneClean, the *Not*I linker was inserted into pTrcHisB/*Sty*I-*Bam*HI by ligation. Restriction analysis with *Bsa*AI-*Not*I confirms the successful construction of pTrcHisB-*Not*I (pTHBN1) by the presence of both 2.5 and 1.8 Kb DNA fragments. Following restriction of pHKO3 with *Eag*I, the 7.7 Kb DNA fragment, containing the six mevalonate pathway orfs, is isolated by agarose gel electrophoresis, purified by GeneClean, and inserted into the *Not*I site of pTHBN1 utilizing directional ligation methodology (Pachuk *et al.*, 2000), thermostable Ampligase® (Epicentre Technologies, Madison, WI), and the bridging oligonucleotides:

3) 5' TTAAATAAGGAGGAATAAACCATGGCGGCCGCAGGAGGAGTTCATAT GTCAGAGTTGAGA 3' (SEQ ID NO: 38); and

4) 5' AACAACAACAACATGACCCGGGATCCGGCCGCGATCCGAGCTCGAGA TCTGCAGCTGGTA 3' (SEQ ID NO: 39);

to form pHKO9 (Fig. 15).

Derivatives of pTHBN1 containing the entire mevalonate pathway plus an additional orf encoding IPP isomerase are constructed as follows: Following restriction of pHKO5 with *Not*I, the 8.2 Kb DNA fragment, containing the six mevalonate pathway orfs plus an orf encoding *R. capsulatus* IPP isomerase, is isolated by agarose gel electrophoresis, purified by GeneClean, and inserted into the *Not*I site of pTHBN1 utilizing directional ligation methodology (Pachuk *et al.*, 2000), thermostable Ampligase® (Epicentre Technologies, Madison, WI), and the bridging oligonucleotides:

5) 5' TCGATTAAATAAGGAGGAATAAACCATGGCGGCCGCAGGAGGAGTTCA TATGTCAGAGTT 3' (SEQ ID NO: 40); and

6) 5' GATTTTCGGATCGATCCTGCGCGGCTGAGCGGCCGCGATCCGAGCTCG AGATCTGCAGCT 3' (SEQ ID NO: 41);

to form pHK10 (Fig. 16). Following restriction of pHKO6 with *Eag*I, the 8.4 Kb DNA fragment, containing the six mevalonate pathway orfs plus an orf encoding *S. pombe* IPP isomerase, is isolated by agarose gel electrophoresis, purified by GeneClean, and inserted into the *Not*I site of pTHBN1 utilizing directional ligation methodology (Pachuk *et al.*, 2000), thermostable Ampligase® (Epicentre Technologies, Madison, WI), and the following bridging oligonucleotides:

7) 5' TCGATTAAATAAGGAGGAATAAACCATGGCGGCCGCAGGAGGAGTTCA TATGTCAGAGTT 3' (SEQ ID NO: 42); and

8) 5' TTCATCGTTGCTAAGGATCCCCCGGGATCCGGCCGCGATCCGAGCTCG AGATCTGCAGCT 3' (SEQ ID NO: 43);

to form pHK11.

Derivatives of pTHBN1 containing only an orf encoding IPP isomerase are constructed as follows: pTHBN1 is restricted with *Not*I and the resulting 5' overhangs are filled in with Klenow and dNTPs. The 4.3 Kb pTHBN1/*Not*I blunt-ended DNA fragment is GeneClean purified. Following restriction of pBSIDI with *Bsa*AI-*Eco*RV, agarose gel electrophoresis and GeneClean purification, the resulting blunt-ended 0.5 Kb DNA fragment containing the *R. capsulatus* IPP isomerase orf is inserted into the filled in *Not*I site of pTHBN1 utilizing chain reaction cloning (Pachuk *et al.*, 2000),

thermostable Ampligase® (Epicentre Technologies, Madison, WI), and the following bridging oligonucleotides:

9) 5' TTAAATAAGGAGGAATAAACCATGGCGGCCGTAAGGAGGCACATATG AGTGAGCTTATAC T 3' (SEQ ID NO: 44); and

10) 5' GCCTGCGCGGCTGAGCGGCCGCGGATCCGATGGCCGCGATCCGAGCTC GAGATCTGCAGCT 3' (SEQ ID NO: 45);

to form pHK12. Following restriction of pIDI with *Bsa*AI-*Sma*I, agarose gel electrophoresis and GeneClean purification, the resulting blunt-ended 0.7 Kb DNA fragment containing the *S. pombe* IPP isomerase orf is inserted into the filled in *Not*I site of pTHBN1 utilizing chain reaction cloning (Pachuk *et al.*, 2000), thermostable Ampligase® (Epicentre Technologies, Madison, WI), and the bridging oligonucleotides:

11) 5' TTAAATAAGGAGGAATAAACCATGGCGGCCGTAGGAGGCACATATGA GTTCCCAACAAGA 3' (SEQ ID NO: 46); and

12) 5' ACCTTAATTCATCGTTGCTAAGGATCCCCCGGCCGCGATCCGAGCTCG AGATCTGCAGCT 3' (SEQ ID NO: 47);

to form pHK13.

Example 14: Increased Isoprenoid Production in Cells Containing the MEP Pathway

In another exemplified embodiment, a carotenoid producing *E. coli* strain is utilized to demonstrate the effect of the insertion of orfs encoding the entire mevalonate pathway, or orfs encoding the entire mevalonate pathway and IPP isomerase, or an orf encoding just IPP isomerase, on production of lycopene as follows: Following the transformation of *E. coli* TOP10 F' (Invitrogen) with pAC-LYC (Cunningham *et al.*, J. Bacteriol. 182:5841-5848, 2000), transformed cells are isolated on LB/Cam (30 μg/ml) plates grown at 30° C. TOP10 F'/pAC-LYC competent cells are prepared by the $CaCl_2$ method (Sambrook *et al.*, 1989) following growth in LB/Cam in darkness at 28° C and 225 rpm to an optical density (A_{600}) of 0.6. Competent TOP10 F'/pAC-LYC cells are transformed with one of the following plasmids: pTrcHisB; pHK09, a pTrcHisB derivative containing the entire mevalonate pathway; pHK10, a pTrcHisB derivative containing the entire mevalonate pathway plus the orf encoding *R. capsulatus* IPP isomerase; pHK11, a pTrcHisB derivative containing the entire mevalonate pathway plus the orf encoding *S. pombe* IPP isomerase; pHK12, a pTrcHisB derivative containing the

orf encoding *R. capsulatus* IPP isomerase; and pHK13, a pTrcHisB derivative containing the orf encoding *S. pombe* IPP isomerase. The bacterial strains described above, comprising pTHBN1 derivatives containing the mevalonate pathway orfs and/or an orf encoding IPP isomerase, are designated HK1, HK2, HK3, HK4, and HK5 respectively. The resulting transformants are isolated as colonies from LB/Cam/amp plates grown at 30° C. Single colonies of TOP10 F'/pAC-LYC/pTrcHisB and HK1 (TOP10 F'/pAC-LYC/pHKO9) are used to individually inoculate 4 ml LB/Cam/amp cultures and grown overnight in the dark at 28° C and 225 rpm. The cultures are serially diluted 10,000 to 100,000-fold, plated on LB/Cam/amp medium containing IPTG, and grown in the dark at rt for 2 to 10 days. The plates are visually examined for an increase in lycopene production as evident by a "darkening" of the light pink colored colonies that are present on the control plates corresponding to TOP10 F'/pAC-LYC/pTrcHisB. The same experiments are performed with strains HK2, HK3, HK4 , and HK5 to determine, visually, the effect of the orfs contained within pHK10, pHK11, pHK12, and pHK13 on lycopene production in TOP10 F'/pAC-LYC cells. The quantification of the carotenoid lycopene in cells, identified as potential overproducers due to their darker color when compared to the color of TOP10 F'/pAC-LYC/pTHBN1 cells, is performed utilizing a spectrophotometric assay as described by Cunningham *et al.* (Cunningham *et al.*, 2000). Increased production of lycopene in *E. coli* cells containing the entire mevalonate pathway or the entire mevalonate pathway plus an additional orf for IPP isomerase establishes that the presence in cells of an additional biosynthetic pathway for the formation of IPP or IPP and DMAPP enhances the production of isoprenoid compounds, such as carotenoids, that are derived from IPP and DMAPP.

Example 15: Demonstration of Antibiotic Resistance Due to the Mevalonate Pathway in MEP Pathway Dependent Cells

In still another exemplified embodiment, *E. coli* cells are transformed with DNA containing orfs, which in their summation comprise the entire mevalonate pathway, and the resulting cells are tested for resistance to the antibiotic fosmidomycin as follows: Following the separate transformation of E. coli TOP10 F' (Invitrogen) with pHKO2, pHKO3 and pHKO9, transformed cells are isolated on LB/Amp (50 μg/ml) plates grown at 30° C. Single colonies of TOP10 F'/pHKO2 (designated strain HK6), TOP10

F'/pHKO3 (designated strain HK7), and TOP10 F'/pHKO9 (designated strain HK8), are used to individually inoculate 4 ml LB/amp cultures and grown overnight at 30° C, 225 rpm. The HK6 and HK7 cultures are serially diluted 10,000 to 100,000-fold and plated on LB containing fosmidomycin (20 μg/ml). The HK8 cultures are serially diluted 10,000 to 100,000-fold and plated on LB/ IPTG containing fosmidomycin (20 μg/ml) Controls are performed with cells comprising TOP10 F' transformed with the parent vectors of pHKO2, pHKO3 and pHKO9, by plating on the appropriate medium containing fosmidomycin establishing that *E. coli* control cells are unable to grow on medium containing fosmidomycin. The ability of transformed *E. coli* cells to grow in the presence of the antibiotic fosmidomycin establishes that the inserted DNA, comprising the entire mevalonate pathway and thus an alternative biosynthetic route to IPP, is functional and can circumvent the inhibition of an enzyme in the trunk line of the MEP pathway.

Example 16: Construction of Plastid Transformation Vectors

In a specific, exemplified embodiment, a plant plastid transformation vector containing a synthetic operon comprising orfs, which in their summation is the entire mevalonate pathway, is constructed as follows: Plasmid pHKO3, a pBluescript derivative containing all six mevalonate pathway orfs, is assembled by restriction of pFCO1 to yield a 3.9 Kb NotI-XhoI DNA fragments containing three mevalonate orfs and its subsequent insertion into the SalI-NotI sites of pHKO1 by directional ligation as described above in Example 8. The plastid transformation vehicle, pHK14 containing the entire mevalonate pathway is constructed as follows: Plastid vector pGS104 (Serino and Maliga, Plant J. 12:687-701, 1997) is restricted with *Nco*I-*Xba*I and the two resulting DNA fragment are separated by agarose gel electrophoresis. Following isolation of the larger DNA fragment by gel excision and its purification by GeneClean, the NcoI-*Xba*I 5' overhangs are dephosphorylated using SAP and filled in with Klenow and dNTPs. The resulting blunt-ended, dephosphorylated DNA fragment derived from pGS104 is GeneClean purified. Following restriction of pHKO3 with EagI, isolation by agarose gel electrophoresis, and purification by GeneClean, the 7.7 Kb DNA fragment is treated with Klenow and dNTPs to fill in the 5' overhangs. The resulting blunt-ended DNA fragment containing the mevalonate pathway is purified by GeneClean and inserted into the

dephosphorylated, Klenow-treated NcoI-XbaI sites of pGS104 by blunt-end ligation to yield pHK14.

Derivatives of pGS104 containing the entire mevalonate pathway plus an additional orf encoding IPP isomerase are constructed as follows: Following restriction of pHKO5 with *Not*I and treatment with Klenow and dNTPs, the resulting 8.2 Kb blunt-ended DNA fragment, containing the six mevalonate pathway orfs plus an orf encoding *R. capsulatus* IPP isomerase, is isolated by agarose gel electrophoresis, purified by GeneClean, and inserted into the dephosphorylated, filled in *Nco*I-XbaI sites of pGS104 by blunt-end ligation to yield pHK15. Following restriction of pHKO6 with EagI and treatment with Klenow and dNTPs, the resulting 8.4 Kb blunt-ended DNA fragment, containing the six mevalonate pathway orfs plus an orf encoding *S. pombe* IPP isomerase, is isolated by agarose gel electrophoresis, purified by GeneClean, and inserted into the dephosphorylated, filled in NcoI-*Xba*I sites of pGS104 by blunt-end ligation to yield pHK16.

Derivatives of pGS104 containing only an orf encoding IPP isomerase are constructed as follows: Following restriction of pBSIDI with *Bsa*AI-*Eco*RV, agarose gel electrophoresis and GeneClean purification, the resulting blunt-ended 0.5 Kb DNA fragment containing the *R. capsulatus* IPP isomerase orf is inserted into the dephosphorylated, filled in *Nco*I-*Xba*I sites of pGS104 by blunt-end ligation to yield pHK17. Following restriction of pIDI with *Bsa*AI-SmaI, agarose gel electrophoresis and GeneClean purification, the resulting blunt-ended 0.7 Kb DNA fragment containing the *S. pombe* IPP isomerase orf is inserted into the dephosphorylated, filled in *Nco*I-*Xba*I sites of pGS104 by blunt-end ligation to yield pHK18.

Example 17: Construction of Transplastomic Plants Containing Orfs Encoding the Mevalonate Pathway or Orfs Encoding the Mevalonate Pathway Coupled with IPP Isomerase

In another exemplified embodiment, tobacco is engineered at the plastid level by using any of the plastid transformation vectors described above, or their equivalents, such as variants of those plastid transformation vectors as can be routinely constructed by means known in the art and containing the orfs as taught and described above. Specifically, *Nicotiana tabacum* var. 'Xanthi NC' leaf sections (1 x 0. 5 cm strips from

in vitro plants with 3 to 5 cm long leaves) are centered in the dish, top side up and bombarded with 1 μm gold micro particles (Kota *et al.*, 1999) coated with DNA containing orfs, which in their summation comprise the entire mevalonate pathway, using a PDS 1000 He device, at 1100 psi. Toxicity is evident in tobacco after three weeks of growth on medium containing the antibiotic fosmidomycin at a concentration of at least 500 micromolar. Transplastomic plants are recovered from leaf sections cultured under lights on standard RMOP shoot regeneration medium or on a Murashige-Skoog salts shoot regeneration medium with 3% sucrose, Gamborg's B5 vitamins, 2 mg/L 6-benzylamino-purine and Phytagel (2.7 g/L), containing 500 μM fosmidomycin for the direct selection of insertion of the entire mevalonate pathway into plastids. Alternatively, the regeneration medium contains an antibiotic, e.g. spectinomycin, for selection based on antibiotic resistance due to any co-transformed gene on the transforming DNA vector, as would be readily apparent to the skilled artisan. De novo green leaf tissue is visible after three weeks. Tissue is removed to undergo a second round of selection on shoot regeneration medium with 500 μM fosmidomycin to encourage homoplasmy and plants are rooted. Genomic DNA is isolated from T0 leaf tissue or T1 leaf tissue derived from in vitro germinated transplastomic seeds utilizing the DNeasy Plant Mini Kit (Qiagen Inc, Valencia, CA) according to the manufacturer's instructions and is subjected to analysis as is known in the art to confirm homoplasmy. The ability to select directly for a transformation event corresponding to the successful insertion of the mevalonate pathway orfs into plastids establishes the use of orfs, which in their summation comprise the entire mevalonate pathway, as a selectable marker for plastid transformation. The construction of fosmidomycin resistant plants establishes the ability of the mevalonate pathway, when functioning in plant plastids, to provide an alternate biosynthetic route to IPP, thus overcoming the effect of an inhibitor targeting an enzyme in the trunk line of the MEP pathway.

Example 18: Metabolic engineering in transplastomic Solanaceae plants

In another exemplified embodiment, Solanaceae species are engineered at the plastid level using infA pseudogene insertion of a selectable marker and orfs for expression. Specifically, leaf sections of a genetically defined white petunia (or other petunia), are engineered, as for the Solanaceous species tobacco (see Example 16), using

vectors pHK04 or pHKO7, or their equivalents, for insertion of orfs encoding the entire mevalonate pathway or orfs encoding the entire mevalonate pathway and IPP isomerase. Transplastomic Solanaceae plants containing orfs encoding the entire mevalonate pathway and IPP isomerase, and containing an additional orf encoding phytoene synthase, are created by insertion of a pBSNT27 (see Example 9) derived vector, constructed as follows:

A Rhodobacter capsulatus orf encoding a polypeptide with phytoene synthase activity is isolated by PCR from genomic DNA using the primers

1) 5' GCGATATCGGATCCAGGAGGACCATATGATCGCCGAAGCGGATATGGA GGTCTGC 3' (sense) (SEQ ID NO: 65)

2) 5' GCGATATCAAGCTTGGATCCTCAATCCATCGCCAGGCCGCGGTCGCGC GC 3' (antisense) (SEQ ID NO: 66)

containing the restriction site BamHI shown underlined. The 1.1 Kb PCR product is isolated by agarose gel electrophoresis, purified by GeneClean and inserted into the pT7Blue-3 vector (Novagen) using the Perfectly Blunt(Cloning Kit (Novagen) according to the manufacturer's instructions. Sequence analysis is performed to identify constructs containing R. capsulatus DNA identical to the published DNA sequence (SEQ ID NO: 71) and are designated pPHS. Following restriction of pPHS with BamHI, isolation by agarose gel electrophoresis, and purification by GeneClean, the 1.1 Kb BamHI DNA fragment containing the orf encoding R. capsulatus phytoene synthase is inserted into the BglII site of pBSNT27 utilizing chain reaction cloning (Pachuk et al., 2000), thermostable Ampligase((Epicentre Technologies, Madison, WI), and the bridging oligonucleotides

3) 5' CTTTCCTGAAACATAATTTATAATCAGATCCAGGAGGACCATATGA TCGCCGAAGCGGAT 3' (SEQ ID NO: 67); and

4) 5' CGACCGCGGCCTGGCGATGGATTGAGGATCTAAACAAACCCGGAA CAGACCGTTGGGAAG 3' (SEQ ID NO: 68);

to create plastid transformation vector pFHO5. Following restriction of pFHO5 with XcmI, a unique site in the infA pseudogene, and purification by GeneClean, the resulting 3' overhangs are removed by treatment with Mung Bean nuclease and the resulting blunt-ended DNA fragment is purified by GeneClean. Vector pFHO3 is restricted with NotI and the resulting 8.3 Kb DNA fragment, containing Operon E, is isolated by agarose gel electrophoresis and purified by GeneClean. The 5' overhangs of the isolated DNA

fragment are filled in with Klenow and dNTPs and the resulting blunt end DNA fragment, containing Operon E, is inserted into the Mung Bean nuclease treated XcmI site of pFHO5 utilizing chain reaction cloning (Pachuk *et al.*, 2000), thermostable Ampligase((Epicentre Technologies, Madison, WI), and the bridging oligonucleotides

5) 5' ATTTTTCATCTCGAATTGTATTCCCACGAAGGCCGCGTCGACTACG GCCGCAGGAGGAGT3' (SEQ ID NO: 69); and

6) 5' TTCGGATCGATCCTGCGCGGCTGAGCGGCCGGAATGGTGAAGTTG AAAAACGAATCCTTC3' (SEQ ID NO: 70);

to create the plastid transformation vector pFHO6 (Fig. 17).

Alternatively, an orf encoding IPP isomerase can be inserted into the XcmI site of pFHO5, utilizing skills as known in the art, to create a plastid transformation vector containing both an orf encoding phytoene synthase and an orf encoding IPP isomerase. Another alternative uses the infA pseudogene as an insertion site for orfs, encoding phytoene synthase, and/or IPP isomerase, and/or the entire mevalonate pathway, linked with the aadA gene as is known in the art for selection of transplastomic plastids on 500 microgram per liter spectinomycin.

The BioRad PDS 1000 He gene gun is used to deliver BioRad tungsten M10 (0.7 micron approx.) microspheres into petunia (Petunia hybrida 'Mitchell') leaves positioned top-side up. Intact leaves, or equivalent tissues of about 6-8 cm^2 per sample are plated onto shoot regeneration medium consisting of Murashige and Skoog basal medium, B5 vitamins, 3% sucrose, 0.7% (w/v) agar and 3 mg/l BA (6-benzylamino-purine), 0.1 mg/l IAA (Deroles and Gardner, Plant Molec. Biol. 11: 355-364, 1988) in 100 x 10 mm plastic Petri dishes. Leaves are centered in the target zone of the gene gun for bombardment at 1100 psi, third shelf from bottom, ~ 5.6 cm gap, 28 mgHg vacuum. M10 microspheres are coated with DNA using standard procedures of $CaCl_2$ and spermidine precipitation, 1.5 to 2 ug DNA/bombardment. After bombardment, tissues are cultured in light in the presence of antibiotic (500 micromolar fosmidomycin). Each leaf sample is then cut into about 6 pieces and cultured on petunia shooting medium containing 500 micromolar fosmidomycin for 3 to 8 weeks, with subculture onto fresh medium every three weeks. Any green shoots are removed and leaves plated onto the same medium containing 500 micromolar fosmidomycin. Plantlets with at least four leaves and of solid green color (no bleaching on petioles or whorls) are transferred for rooting onto solidified hormone-free

Murashige and Skoog salts with B5 vitamins and 2% sucrose and are grown to flowering. The dependency of increased carotenoid production in Solanacae on the combination of the orfs inserted, be it an orf encoding phytoene synthase alone; or orfs encoding the entire mevalonate pathway and phytoene synthase; or orfs encoding phytoene synthase, the entire mevalonate pathway and IPP isomerase; or orfs for phytoene synthase and IPP isomerase, establishes that the addition of the mevalonate pathway and/or IPP isomerase to plant plastids enhances the production of isoprenoid compounds that are derived from IPP and DMAPP; and the suitability of a pseudogene insertion site for creating transplastomic Petunia.

Example 19: Transformation of microalgae

In a specific exemplified embodiment, chloroplast transformants are obtained by microprojectile bombardment of Chlamydomonas reinhardtii cells and subsequent selection on fosmidomycin. Specifically, a genecluster containing the complete mevalonate pathway is substituted, as a selectable marker, for the coding sequence of the aadA gene in the pUC18 derived vector containing 5-atpA:aadA:rbcL-3 (Goldschmidt-Clermont M., Nucleic Acids Res. 19:4083-4089, 1991) as follows: Plasmid pUC-atpX-AAD is restricted with NcoI, purified by GeneCleanand treated with Mung Bean nuclease to remove the resulting 5' overhangs. Following GeneClean purification, the blunt ended DNA fragment is restricted with HindIII to remove the aadA orf and the remaining DNA fragment, containing approximately 653 base pairs of the C. reinhardtii atpA gene and approximately 437 base pairs of the C. reinhardtii rbcL gene (Goldschmidt-Clermont M., 1991), is isolated by agarose gel electrophoresis and purified by GeneClean. Plasmid pFHO4 is restricted with NdeI, purified by GeneClean, and the resulting 5 overhangs are filled in with Klenow and dNTPs. Following GeneClean purification, the blunt ended DNA fragment is restricted with HindIII and the resulting DNA fragment, containing Operon F (see Fig. 13), is isolated by agarose gel electrophoresis and purified by GeneClean. The blunt end-HindIII fragment is inserted into the blunt end HindIII sites of the DNA fragment isolated from pUC-atpX-AAD by ligation resulting in the orf encoding S. cerevisiae acetoacetylCoA thiolase, located at the beginning of Operon F, to be in frame with the ATG start codon of the 5atpA DNA in pUC-atpX-AAD (Goldschmidt-Clermont M., 1991). The resulting modified yeast orf

only encodes 2 extra amino acids, Met and Ser, appended to the N-terminal Met of the acetoacetylCoA thiolase polypeptide encoded by Operon F. The resulting chlamydomonas plastid transformation vector is designated pHK19. About 10,000 cells are spread on TAP plates containing 200 micromolar fosmidomycin, plates are dried, and then cells are immediately bombarded with M10 or 1 micron gold particles coated with about 2 micrograms of plasmid DNA using the PDS-1000 He gene gun, 1100 psi, fourth shelf from bottom, ~ 2 cm gap, ~28 mgHg vacuum (alternatively cells are spread over a Nytran nylon 0.45 micron membrane placed on top of TAP agar and bombarded without a drying phase). Plates are incubated in low light for two to three weeks before colonies are counted. Fosmidomycin-resistant colonies are green (vs yellowish for susceptible cells) and transformants are characterized using skills as known in the art. This demonstrates use of orfs encoding the entire mevalonate pathway as a selectable marker for green algae and by virtue of its functioning demonstrates its utility for overproduction of isoprenoid metabolites in microalgae.

Example 20: Metabolic engineering in transplastomic grain crops (rice)

In another exemplified embodiment, an operon comprising orfs encoding the entire mevalonate pathway are inserted into the plastids of rice as follows: A DNA fragment isolated from pHKO3, containing the complete mevalonate pathway, or from pFHO2, containing orfs encoding the entire mevalonate pathway and IPP isomerase, is inserted into the NcoI-XbaI sites of plasmid pMSK49 to replace the gfp coding region adjacent to the coding region for streptomycin resistance, aadA; or inserted into the BstXI-NcoI digested DNA of plasmid pMSK48 using skills as is known in the art for direct selection on fosmidomycin. The resulting plasmids contain rice-specific insertion sequences of pMSK35 as described in Khan and Maliga, Nature Biotechnology 17: 910-914, 1999. Embryonic suspensions, induced as previously described (Khan and Maliga 1999), of japonica rice *Oryza sativa* 'Taipei 309' engineered with the beta-carotene pathway (Ye *et al.* Science 287:303-305) are plated into filter paper and bombarded with the PDS1000 He device as described in Example 17. After two days on non-selective medium and then one to two weeks in selective AA medium (Toriyama and Hinata, Plant Science 41: 179-183, 1985) tissue is transferred to agar solidified medium of MS salts, and vitamins, 100mg/L myo-inositol, 4 mg/L 6-benzylaminopurine, 0.5 mg/L

indoleacetic acid, 0.5 mg/L1-napthaleneacetic acide, 3% sucrose, 4% maltose and 100 mg/L streptomycin sulfate or 500 μM fosmidomycin. Transplastomic shoots appear following cultivation in the light after three weeks and leaf samples are analyzed for the operon by PCR.

REFERENCES CITED

U.S. Patent Documents

Adang et al., "Synthetic Insecticidal Crystal Protein Gene," US patent 5,380,831 (1995)

Chappel et al., "Process for Composition for Increasing Squalene and Sterol Accumulation in Higher Plants," US patent 5,349,126 (1994)

Fujimoto et al., "Synthetic Insecticidal Gene, Plants of the Genus Oryza Transformed with the Gene, and Production Thereof," US patent 5,436,391 (1995)

Kamuro et al. "Herbicide" US Patent 4,846,872 (1989)

Other References

Albrecht et al., "Novel Hydroxycarotenoids with Improved Antioxidative Properties Produced by Gene Combination in Escherichia coli," Nature Biotech. 18:843 - 846 (2000)

Allison et al., MDMV Leader (Maize Dwarf Mosaic Virus) Virology 154:9-20 (1986)

Altschul et al., J. Mol. Biol. 215:403-410 (1990)

Ashby and Edwards, "Elucidation of the Deficiency in Two Yeast Coenzyme Q Mutants: Characterization of the Structural Gene Encoding Hexaprenyl Pyrophosphate Synthetase," J. Biol. Chem. 265:13157-13164 (1990)

Ballas et al., Nucleic Acids Res. 17:7891-7903 (1989)

Beaucage and Caruthers, Tetra. Letts., 22:1859-1862 (1981)

Bock and Hagemann, "Extranuclear Inheritance: Plastid Genetic: Manipulation of Plastid Genomes and Biotechnological Application," Prog. Bot. 61:76-90 (2000)

Boyton and Gillham, "Chloroplast Transformation in Chlamydomoas," Methods Enzymol. 217:510-536 (1993)

Clarke, "Protein Isoprenylation and Methylation at Carboxy-terminal Cysteine Residues," Annu. Rev. Biochem. 61:355-386 (1992)

Cunningham and Gantt, "Genes and Enzymes of Carotenoid Biosynthesis in Plants," Ann. Rev. Plant Mol. Biol. 39:475-502 (1998)

Cunningham et al., "Evidence of a Role for LytB in the Nonmevalonate Pathway of Isoprenoid Biosyhthesis," J. Bacteriol. 182:5841-5848 (2000)

Dale, P.J., "Spread of Engineered Genes to Wild Relatives," Plant Physiol. 100:13-15

(1992)

Daniell et al., "Containment of Herbicide Resistance Through Genetic Engineering of the Chloroplast Genome," Nat. Biotechnol. 16:345-348 (1998)

del Campo et al, Plant Physiol 114:748 (1997)

Della-Cioppa et al., Plant Physiol. 84:965-968 (1987)

Deroles and Gardner, "Expression and Inheritance of Kanamycin Resistance in a large Number of Transgenic Petunias Generated by Agrobacterium-Mediated Transformation," Plant Molec. Biol. 11: 355-364 (1988)

Eisenreich et al., "The Deoxyxylulose Phosphate Pathway of Terpenoid Biosynthesis in Plants and Microorganisms," Chemistry and Biology 5:R221-R233 (1998)

Elroy-Stein et al., PNAS USA 86:6126-6130 (1989)

Gallie et al., in Molecular Biology of RNA, ed. Cech, (Liss, New York) 237-256 (1989)

Garrett et al., "Accumulation of a Lipid A Precursor Lacking the 4'-Phosphate following Inactivation of the Escherichia coli lpxK Gene," J. Biol. Chem. 273:12457-12465 (1998)

Goldschmidt-Clermont M., "Transgenic Expression of Aminoglycoside Adenine Transferase in the Chloroplast: A Selectable Marker for Site-directed Transformation of Chlamydomonas," Nucleic Acids Res.19:4083-4089 (1991)

Goodwin, "Biosynthesis of Carotenoids and Plant Triterpenes: the Fifth CIBA Medal Lecture," Biochem. J. 123:293-329 (1971)

Guda et al., "Stable Expression for a Biodegradable Protein Based Polymer in Tobacco Chloroplasts," Plant Cell Reports 19:257-262 (2000)

Guerineau et al., Mol. Gen. Genet. 262:141-144 (1991)

Hahn et al., "1-Deoxy-D-Xylulose 5-Phosphate Synthase, the Gene Product of Open Reading Frame (ORF) 2816 and ORF2895 in Rhodobacter capsulatus," J. Bacteriol. 183:1-11 (2001)

Hahn and Poulter, "Isolation of Schizosaccharomyces pombe Isopentenyl Diphosphate Isomerase cDNA Clones by Complementation and Synthesis of the Enzyme in Escherichia coli," J. Biol. Chem. 270:11298-11303 (1995)

Hahn et al., "Escherichia coli Open Reading Frame 696 Is idi, a Nonessential Gene Encoding Isopentenyl Diphosphate Isomerase," J. Bacteriol. 181:4499-4504 (1999)

Hahn et al., "Open Reading Frame 176 in the Photosynthesis Gene Cluster of Rhodobacter capsulatus Encodes idi, a Gene for Isopentenyl Diphosphate Isomerase," J. Bacteriol. 178:619-624 (1996)

Hamilton et al., "New Method for Generating Deletions and Gene Replacements in Escherichia coli," J. Bacteriol. 171:4617-4622 (1989)

Harker and Bramley, "Expression of Prokaryotic 1-Deoxy-D-Xylulose 5-Phosphates in Escherichia coli Increases Carotenoid and Ubiquinone Biosynthesis," FEBS Letters 448:115-119 (1999)

Herz et al., "Biosynthesis of Terpenoids: YgbB Protein Converts 4-Diphosphocytidyl-2C-Methyl-D-Erythritol 2-Phosphate to 2C-Methyl-D-Erythritol 2,4-Cyclodiphosphate," Proc. Natl. Acad. Sci. USA 97:2486-2490 (2000)

Jobling et al., Nature 325:622-625 (1987)

Joshi et al., Nucleic Acid Res. 15:9627-9639 (1987)

Kajiwara et al., "Expression of an Exogenous Isopentenyl Diphosphate Isomerase Gene Enhances Isoprenoid Biosynthesis in Escherichia coli," Biochem. J. 324:421-426 (1997)

Kavanagh et al., "Homeologous Plastid DNA Transformation in Tobacco is Mediated by Multiple Recombination Events," Genetics 152:1111-1122 (1999)

Keeler et al., "Movement of Crop Transgenes into Wild Plants," in Herbicide Resistant Crops: Agricultural, Economic, Environmental, Regulatory and Technological Aspects, (S.O. Duke, ed.) CRC Press, Boca Rotan, FL, pp 303-330 (1996)

Khan and Maliga, "Fluorescent Antibiotic Resistance Marker for Tracking Plastid Transformation in Higher Plants," Nature Biotech. 17:910-914 (1999)

Kota et al., "Overexpression of the Bacilllus thuringiensis (Bt) Cry2Aa2 Protein in Chloroplasts Confers Resistance to Plants Against Susceptible and Bt-resistant Insects," Proc. Natl. Acad. Sci. USA 96:1840-1845 (1999)

Kunkel, Proc. Natl. Acad. Sci. USA 82:488-492 (1985)

Kunkel et al., Methods and Enzymol; 154:367-382 (1987)

Kuzuyama et al., "Direct Formation of 2-C-Methyl-D-Erythritol 4-Phosphate by 1-Deoxy-D-Xylulose 5-Phosphate Reductoisomerase, a New Enzyme in the Non-Mevalonate Pathway to Isopentenyl Diphosphate," Tetrahedron Lett. 39:4509-4512 (1998)

Kuzuyama et al., "Fosmidomycin, a Specific Inhibitor of 1-Deoxy-D-Xylulose 5-

Phosphate Reductoisomerase in the Nonmevalonate Pathway for Terpenoid Biosynthesis," Tetrahedron Lett. 39:7913-7916 (1998)

Kuzuyama et al., "An Unusual Isopentenyl Diphosphate Isomerase Found in the Mevalonate Pathway Gene Cluster from Streptomyces sp. strain CL190," Proc. Natl. Acad. Sc.i USA 98:932-7 (2001)

Lange and Croteau, "Isopentenyl diphosphate biosynthesis via a mevalonate independent pathway: Isopentenyl monophosphate kinase catalyzes the terminal enzymatic step," Proc. Natl. Acad. Sci. USA 96:13714-13719 (1999)

Lichtenthaler et al., "Biosynthesis of Isoprenoids in Higher Plant Chloroplasts Proceeds via a Mevalonate-Independent Pathway," FEBS Letters 400:271-274 (1997)

Lois et al,. "Cloning and Characterization of a Gene from Escherichia coli Encoding a Transketolase-Like Enzyme that Catalyzes the Synthesis of D-1-Deoxyxylulose 5-Phosphate, a Common Precursor for Isoprenoid, Thiamin, and Pyridoxol Biosynthesis," Proc. Natl. Acad. Sci. USA 95:2105-2110 (1998)

Lommel et al., Virology 81:382-385 (1991)

Lüttgen et al., "Biosynthesis of Terpenoids: YchB Protein of Escherichia coli Phosphorylates the 2-Hydroxy Group of 4-Diphosphocytidyl-2-C-Methyl-D-Erythritol," Proc. Natl. Acad. Sci. USA 97:1062-1067 (2000)

Macejak et al., Nature 353:90-94 (1991)

Mann et al., "Metabolic Engineering of Astaxanthin Production in Tobacco Flowers," Nature Biotech. 18:888-892 (2000)

Martin et al., "Gene Transfer to the Nucleus and the Evolution of Chloroplasts," Nature 393:162-165 (1998)

Matsuoka et al., "Variable Product Specificity of Microsomal Dehydrodolichyl Diphosphate Synthase from Rat Liver," J. Biol. Chem. 266:3464-3468 (1991)

Matteuci et al., J. Am. Chem. Soc., 103: 3185 (1981)

Meinkoth and Wahl, Anal. Biochem. 138:267-284 (1984)

Meyer and Saedler, "Homology-Dependent Gene Silencing in Plants,"Ann. Rev. Plant. Physiol. Mol. Biol. 47:23-48 (1996)

Millen et al., "Many Parallel Losses of infA from Chloroplast DNA During Angiosperm Evolution with Multiple Independent Transfers to the Nucleus," Plant Cell 13: 645-658 (2001)

Mogen et al., Plant Cell 2:1261-1272 (1990)

Munroe et al., Gene 91:151-158 (1990)

Murray et al., Nucleic Acids Res. 17:477-498 (1989)

Needleman et al., J. Mol. Biol. 48:443 (1970)

Newman et al., "Genes Galore: A Summary of Methods for Accessing Results from Large-Scale Partial Sequencing of Anonymous Arabidopsis cDNA Clones," Plant Physiology 106:1241-1255 (1994)

Nielsen and Bloor, "Analysis and Developmental Profile of Carotenoid Pigments in Petals of Three Yellow Petunia Cultivars," Scientia Hort. 71:257-266 (1997)

Pachuk et al., Gene 243:19-25 (2000)

Pearson et al., Proc. Natl. Acad. Sci. 85:2444 (1988)

Popjak, "Natural Substances Formed Biologically from Mevalonic Acid," Biochemical symposium no. 29 (T. W. Goodwin, ed.) Academic Press, New York, pp 17-37. (1970)

Proudfoot, Cell 64:671-674 (1991)

Ramos-Valdivia et al., "Isopentenyl Diphosphate Isomerase: A Core Enzyme in Isoprenoid Biosynthesis: A Review of its Biochemistry and Function," Nat. Prod. Rep. 6:591-603 (1997)

Rohdich et al., "Cytidine 5'-Triphosphate-Dependent Biosynthesis of Isoprenoids: YgbP Protein of Escherichia coli Catalyzes the Formation of 4-Diphosphocytidyl-2-C-methylerythritol," Proc. Natl. Acad. Sci. USA 96:11758-11763 (1999)

Sambrook et al., "Molecular Cloning: A Laboratory Manual," 2nd ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY (1989)

Sanfacon et al., Genes Dev. 5:141-149 (1991)

Serino and Maliga, "A Negative Selection Scheme Based on the Expression of Cytosine Deaminase in Plastids," Plant J. 12:687-701 (1997)

Smith et al., Adv. Appl. Math. 2:482 (1981)

Sprenger et al., "Identification of a Thiamin-Dependent. Synthase in Escherichia coli Required for the Formation of the 1-Deoxy-D-Xylulose 5-Phosphate Precursor to Isoprenoids, Thiamin, and Pyridoxol," Proc. Natl. Acad. Sci. USA 94:12857-12862 (1997)

Stevens and Burton, "Genetic Engineering of Eukaryotic Algae: Progress and prospects," J. Phycol 33:713-722 (1997)

Sugiura, M., "Direct submission to the EMBL/GenBank/DDBJ databases, bases 1-155939," (1986)

Takagi et al., "A Gene Cluster for the Mevalonate Pathway from Streptomyces sp Strain CL190," J. Bacteriol. 182:4153-4157 (2000)

Takahashi, et al., "Purification, Characterization, and Cloning of a Eubacterial 3-Hydroxy-3-Methylglutaryl Coenzyme A Reductase, a Key Enzyme Involved in Biosynthesis of Terpenoids," J. Bacteriol. 181:1256-1263 (1999)

Toriyama and Hinata, "Cell Suspension and Protoplast Culture in Rice," Plant Science 41:179-183 (1985)

Tsudsuki, T., "Direct submission, bases 1-155939. Data Processing Center, Aichi-Gakuin University, Aichi, Japan," (1998)

Vasil et al., in Cell Culture and Somatic Cell Genetics of Plants, Vols. I, II, and III, Laboratory Procedures and Their Applications (Academic press) (1984)

Weissbach et al., Methods for Plant Mol. Biol. (1989)

Ye et al., Science 287:303-30 (2000)

Claims

1. A method of providing a cell with herbicide resistance comprising the steps of:

providing a polynucleotide comprising polynucleotide sequences encoding the enzymes of the complete mevalonate pathway;

introducing said polynucleotide into a plurality of target cells;

contacting said cells with an herbicide that targets a component of a non-mevalonate pathway; and

selecting at least one target cell which exhibits herbicide resistance.

2. The method according to claim 1, wherein said target cell is a plant cell.

3. The method according to claim 1, wherein said target cell is a microalgae cell.

4. The method according to claim 2, wherein said polynucleotide is introduced into a plastid of said target cell.

5. The method according to claim 3, wherein said polynucleotide is introduced into a plastid of said target cell.

6. The method according to claim 1, wherein said polynucleotide further comprises a sequence encoding IPP isomerase.

7. The method according to claim 2, wherein said polynucleotide comprises a sequence encoding IPP isomerase.

8. The method according to claim 3, wherein said polynucleotide comprises a sequence encoding IPP isomerase.

9. The method according to claim 4, wherein said polynucleotide comprises a sequence encoding IPP isomerase.

10. The method according to claim 5, wherein said polynucleotide comprises a sequence encoding IPP isomerase.

11. An isolated polynucleotide encoding *R. capsulatus* IPP isomerase, said polynucleotide comprising the sequence of SEQ ID NO: 55.

12. A method for producing a transformed plant comprising the steps of:

providing a polynucleotide comprising polynucleotide sequences encoding the enzymes of the complete mevalonate pathway;

introducing said polynucleotide into a plurality of target plant cells;

selecting at least one plant cell transformed with said polynucleotide; and

regenerating said at least one plant cell into a transformed plant.

13. A method according to claim 12, wherein said polynucleotide is introduced into a plastid of said target plant cell, and wherein said plant is a transplastomic plant.

14. A plant produced by the method of claim 11.

15. A plant according to claim 14, wherein said plant is a transplastomic plant.

16. A method for providing transformed cells having increased isoprenoid production as compared to non-transformed cells, comprising the steps of:

providing an isolated polynucleotide comprising polynucleotide sequences encoding the enzymes of the complete mevalonate pathway;

providing a plurality of target cells;

introducing said isolated polynucleotide into said target cells;

selecting target cells which have been transformed with said polynucleotide; and

growing said transformed cells under conditions whereby additional generations of descendant transformed cells are produced, said transformed cells exhibiting increased isoprenoid production as compared to non-transformed cells of the same type.

17. The method according to claim 16, wherein said isolated polynucleotide

further comprises the polynucleotide sequence encoding IPP isomerase.

18. The method of claim 16, wherein said target cells are microalgae.

19. The method of claim 17, wherein said target cells are microalgae.

20. The method of claim 16, further comprising the step of regenerating said transformed cells into a transformed plant, wherein said transformed plant exhibits increased isoprenoid production as compared to a non-transformed plant of the same type.

21. A plant produced by the method of claim 20.

22. Descendants of the plant of claim 21, wherein said descendants exhibit increased isoprenoid production as compared to non-transformed plants of the same type.

23. A method of providing a cell with antibiotic resistance comprising the steps of:

providing a polynucleotide comprising polynucleotide sequences encoding the enzymes of the complete mevalonate pathway;

introducing said polynucleotide into a plurality of target cells;

contacting said cells with an antibiotic that targets a component of a non-mevalonate pathway; and

selecting at least one target cell which exhibits antibiotic resistance.

24. The method according to claim 23, wherein said target cell is a plant cell.

25. The method according to claim 24, wherein said target cell is a microalgae cell.

26. The method according to claim 24, wherein said polynucleotide is introduced into a plastid of said target cell.

27. The method according to claim 25, wherein said polynucleotide is introduced into a plastid of said target cell.

28. The method according to claim 23, wherein said polynucleotide further comprises a sequence encoding IPP isomerase.

29. The method according to claim 24, wherein said polynucleotide comprises a sequence encoding IPP isomerase.

30. The method according to claim 25, wherein said polynucleotide comprises a sequence encoding IPP isomerase.

31. The method according to claim 26, wherein said polynucleotide comprises a sequence encoding IPP isomerase.

32. The method according to claim 27, wherein said polynucleotide comprises a sequence encoding IPP isomerase.

33. The method according to claim 1, wherein said polynucleotide comprises the polynucleotide sequence of SEQ ID NO: 58.

34. The method according to claim 1, wherein said polynucleotide comprises the polynucleotide sequence of SEQ ID NO: 59.

35. The method according to claim 1, wherein said polynucleotide comprises the polynucleotide sequence of SEQ ID NO: 60.

36. The method according to claim 1, wherein said polynucleotide comprises the polynucleotide sequence of SEQ ID NO: 61.

37. The method according to claim 1, wherein said polynucleotide comprises the

polynucleotide sequence of SEQ ID NO: 62.

38. The method according to claim 1, wherein said polynucleotide comprises the polynucleotide sequence of SEQ ID NO: 63.

39. The method according to claim 1, wherein said polynucleotide comprises the polynucleotide sequence of SEQ ID NO: 64.

40. The method according to claim 1, wherein said polynucleotide comprises the polynucleotide sequence of SEQ ID NO: 72.

41. The method according to claim 1, wherein said polynucleotide comprises the polynucleotide sequence of SEQ ID NO: 73.

42. The method according to claim 1, wherein said polynucleotide comprises the polynucleotide sequence of SEQ ID NO: 74.

43. The method according to claim 1, wherein said polynucleotide comprises the polynucleotide sequence of SEQ ID NO: 76.

44. The method according to claim 12, wherein said polynucleotide comprises the polynucleotide sequence of SEQ ID NO: 58.

45. The method according to claim 12, wherein said polynucleotide comprises the polynucleotide sequence of SEQ ID NO: 59.

46. The method according to claim 12, wherein said polynucleotide comprises the polynucleotide sequence of SEQ ID NO: 60.

47. The method according to claim 12, wherein said polynucleotide comprises the polynucleotide sequence of SEQ ID NO: 61.

48. The method according to claim 12, wherein said polynucleotide comprises the polynucleotide sequence of SEQ ID NO: 62.

49. The method according to claim 12, wherein said polynucleotide comprises the polynucleotide sequence of SEQ ID NO: 63.

50. The method according to claim 12, wherein said polynucleotide comprises the polynucleotide sequence of SEQ ID NO: 64.

51. The method according to claim 12, wherein said polynucleotide comprises the polynucleotide sequence of SEQ ID NO: 72.

52. The method according to claim 12, wherein said polynucleotide comprises the polynucleotide sequence of SEQ ID NO: 73.

53. The method according to claim 12, wherein said polynucleotide comprises the polynucleotide sequence of SEQ ID NO: 74.

54. The method according to claim 12, wherein said polynucleotide comprises the polynucleotide sequence of SEQ ID NO: 76.

55. The method according to claim 16, wherein said polynucleotide comprises the polynucleotide sequence of SEQ ID NO: 58.

56. The method according to claim 16, wherein said polynucleotide comprises the polynucleotide sequence of SEQ ID NO: 59.

57. The method according to claim 16, wherein said polynucleotide comprises the polynucleotide sequence of SEQ ID NO: 60.

58. The method according to claim 16, wherein said polynucleotide comprises

the polynucleotide sequence of SEQ ID NO: 61.

59. The method according to claim 16, wherein said polynucleotide comprises the polynucleotide sequence of SEQ ID NO: 62.

60. The method according to claim 16, wherein said polynucleotide comprises the polynucleotide sequence of SEQ ID NO: 63.

61. The method according to claim 16, wherein said polynucleotide comprises the polynucleotide sequence of SEQ ID NO: 64.

62. The method according to claim 16, wherein said polynucleotide comprises the polynucleotide sequence of SEQ ID NO: 72.

63. The method according to claim 16, wherein said polynucleotide comprises the polynucleotide sequence of SEQ ID NO: 73.

64. The method according to claim 16, wherein said polynucleotide comprises the polynucleotide sequence of SEQ ID NO: 74.

65. The method according to claim 16, wherein said polynucleotide comprises the polynucleotide sequence of SEQ ID NO: 76.

66. The method according to claim 23, wherein said polynucleotide comprises the polynucleotide sequence of SEQ ID NO: 58.

67. The method according to claim 23, wherein said polynucleotide comprises the polynucleotide sequence of SEQ ID NO: 59.

68. The method according to claim 23, wherein said polynucleotide comprises the polynucleotide sequence of SEQ ID NO: 60.

69. The method according to claim 23, wherein said polynucleotide comprises the polynucleotide sequence of SEQ ID NO: 61.

70. The method according to claim 23, wherein said polynucleotide comprises the polynucleotide sequence of SEQ ID NO: 62.

71. The method according to claim 23, wherein said polynucleotide comprises the polynucleotide sequence of SEQ ID NO: 63.

72. The method according to claim 23, wherein said polynucleotide comprises the polynucleotide sequence of SEQ ID NO: 64.

73. The method according to claim 23, wherein said polynucleotide comprises the polynucleotide sequence of SEQ ID NO: 72.

74. The method according to claim 23, wherein said polynucleotide comprises the polynucleotide sequence of SEQ ID NO: 73.

75. The method according to claim 23, wherein said polynucleotide comprises the polynucleotide sequence of SEQ ID NO: 74.

76. The method according to claim 23, wherein said polynucleotide comprises the polynucleotide sequence of SEQ ID NO: 76.

77. An isolated polynucleotide comprising polynucleotide sequences encoding the enzymes of the complete mevalonate pathway, said polynucleotides comprising a sequence selected from the group consisting of SEQ ID NO: 58, SEQ ID NO: 59, SEQ ID NO: 60, SEQ ID NO: 61, SEQ ID NO: 62, SEQ ID NO: 63, SEQ ID NO: 64, SEQ ID NO: 72, SEQ ID NO: 73, SEQ ID NO: 74, and SEQ ID NO: 76.

78. An isolated polynucleotide according to claim 77, wherein said polynucleotide comprises the sequence of SEQ ID NO: 58.

79. An isolated polynucleotide according to claim 77, wherein said polynucleotide comprises the sequence of SEQ ID NO: 59.

80. An isolated polynucleotide according to claim 77, wherein said polynucleotide comprises the sequence of SEQ ID NO: 60.

81. An isolated polynucleotide according to claim 77, wherein said polynucleotide comprises the sequence of SEQ ID NO: 61.

82. An isolated polynucleotide according to claim 77, wherein said polynucleotide comprises the sequence of SEQ ID NO: 62.

83. An isolated polynucleotide according to claim 77, wherein said polynucleotide comprises the sequence of SEQ ID NO: 63.

84. An isolated polynucleotide according to claim 77, wherein said polynucleotide comprises the sequence of SEQ ID NO: 64.

85. An isolated polynucleotide according to claim 77, wherein said polynucleotide comprises the sequence of SEQ ID NO: 72.

86. An isolated polynucleotide according to claim 77, wherein said polynucleotide comprises the sequence of SEQ ID NO: 73.

87. An isolated polynucleotide according to claim 77, wherein said polynucleotide comprises the sequence of SEQ ID NO: 74.

88. An isolated polynucleotide according to claim 77, wherein said

polynucleotide comprises the sequence of SEQ ID NO: 76.

89. An isolated polynucleotide comprising the sequence of SEQ ID NO: 75.

90. A method of providing a cell with an inserted polynucleotide sequence encoding one or more products of interest comprising the steps of:

providing a plurality of target cells having an identified pseudogene site therein;

providing an isolated polynucleotide comprising polynucleotide sequences of said pseudogene site flanking at least one coding sequence of interest;

introducing said polynucleotide into a plurality of said target cells;

selecting at least one target cell which contains the coding sequence of interest inserted into said pseudogene site .

91. The method according to claim 90, wherein said pseudogene is a defunct gene located in an active operon from which monocistronic or polycistronic RNA is produced.

92. The method according to claim 91, wherein said operon is the *rpl23* operon .

93. The method according to claim 91, wherein said pseudogene is *infA*.

94. The method according to claim 90, wherein the inserted polynucleotide is operably linked to the regulatory sequences of the pseudogene.

95. The method according to claim 94, wherein the inserted polynucleotide is operably linked to the regulatory sequences of the *rpl23* operon.

96. The method according to claim 94, wherein the inserted polynucleotide is operably linked to the regulatory sequences of *infA*.

97. The method according to claim 90, wherein the isolated polynucleotide further comprises additional flanking sequences that themselves flank the pseudogene sequences, and wherein said additional flanking sequences, in their native state, flank the pseudogene in its native state.

98. The method according to claim 97, wherein the inserted polynucleotide replaces the pseudogene in its entirety.

99. The method according to claim 97, wherein said additional flanking sequences are native plastid sequences.

100. The method according to claim 90, wherein said target cell is a plant cell.

101. The method according to claim 90, wherein said target cell is a microalgae cell.

102. The method according to claim 100, wherein said polynucleotide is introduced into a plastid of said target cell.

103. The method according to claim 101, wherein said polynucleotide is introduced into a plastid of said target cell.

104. The method according to claim 100, wherein said plant cell is selected from the group consisting of the rosids, asterids, and liliales.

105. The method according to claim 100, wherein said plant cell is from a solanaceous species.

106. The method according claim 105, wherein said plant cell is selected from the group consisting of petunia, tomato, potato, and tobacco cells.

107. The method according to claim 90, wherein said coding sequence of interest comprises polynucleotide sequences encoding the enzymes of the complete mevalonate pathway.

108. The method according to claim 90, wherein said polynucleotide further comprises a sequence encoding IPP isomerase.

109. The method according to claim 107, wherein said polynucleotide further comprises a sequence encoding IPP isomerase.

110. The method according to claim 90, wherein said polynucleotide comprises polynucleotide sequences encoding phytoene synthase.

111. The method according to claim 90, wherein said polynucleotide is promoterless.

112. A method according to any of claims 100, 102, 104, 105, and 106, said method further comprising the step of regenerating said selected target cell into a plant, said plant comprising said coding sequence of interest.

113. A plant produced by the method of claim 112.

114. Descendants of the plant of claim 113, said descendant plants comprising said coding sequence of interest.

Fig. 1

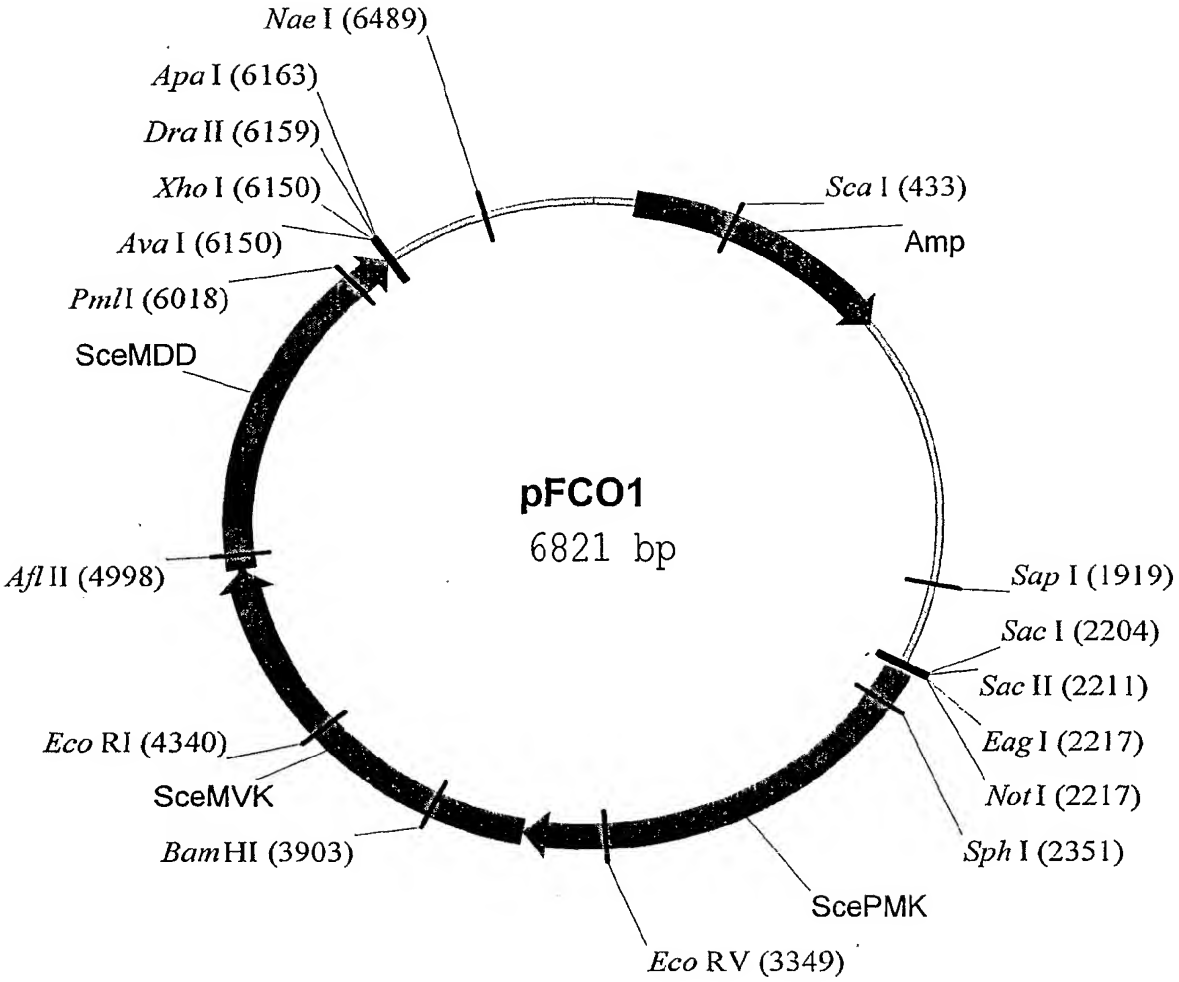

Nae I (6489)
Apa I (6163)
Dra II (6159)
Xho I (6150)
Ava I (6150)
PmlI (6018)
SceMDD
Afl II (4998)
Eco RI (4340)
SceMVK
Bam HI (3903)
Eco RV (3349)
ScePMK
Sph I (2351)
Not I (2217)
Eag I (2217)
Sac II (2211)
Sac I (2204)
Sap I (1919)
Amp
Sca I (433)
pFCO1
6821 bp

Fig. 2

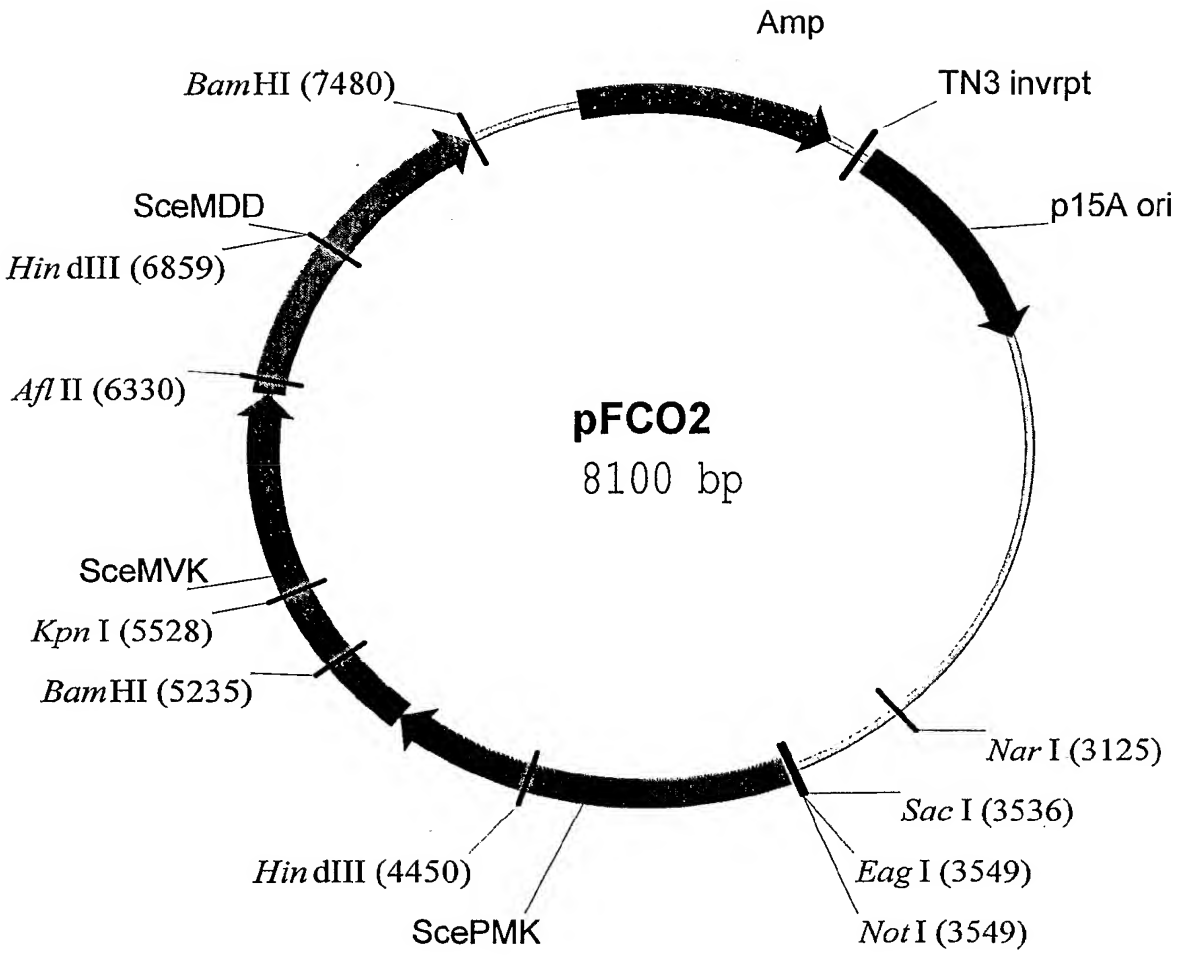

Amp
TN3 invrpt
p15A ori
Nar I (3125)
Sac I (3536)
Eag I (3549)
Not I (3549)
ScePMK
Hin dIII (4450)
Bam HI (5235)
Kpn I (5528)
SceMVK
Afl II (6330)
Hin dIII (6859)
SceMDD
Bam HI (7480)
pFCO2
8100 bp

Fig. 3

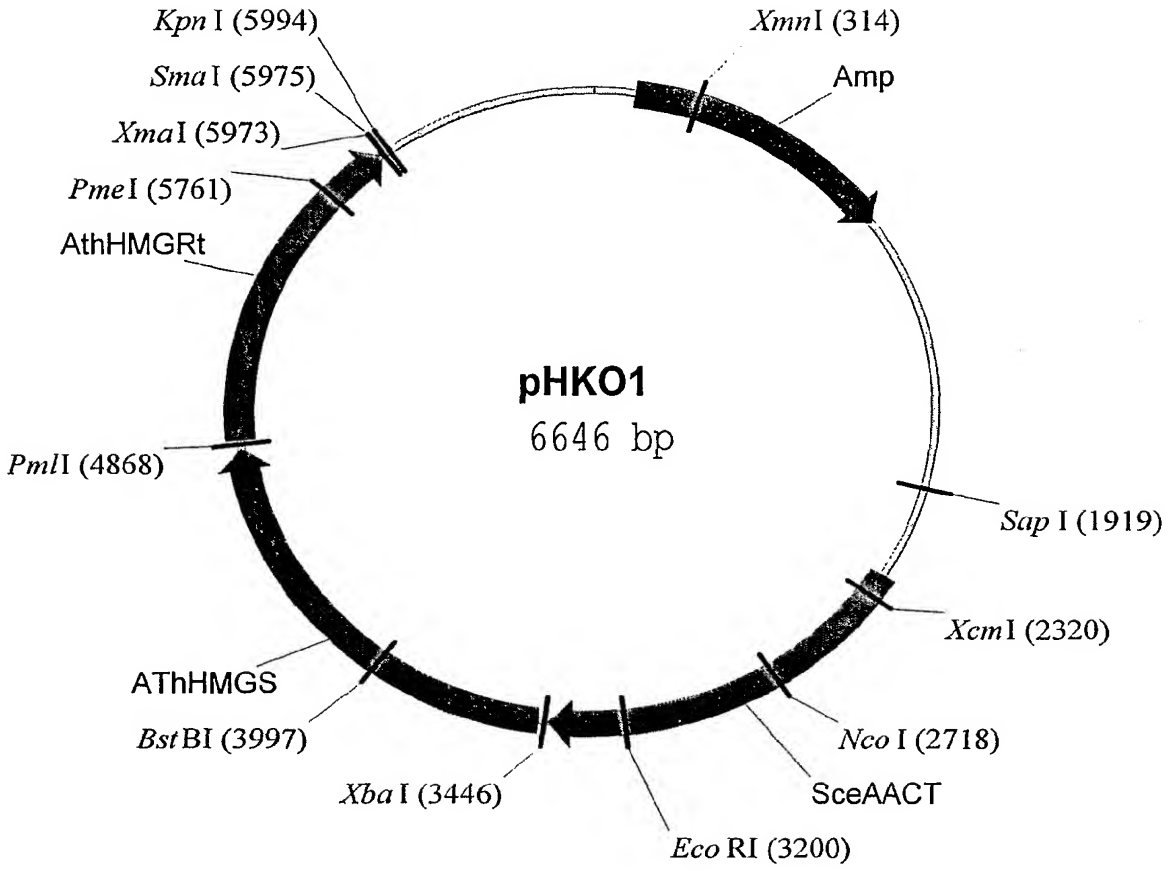

Kpn I (5994)
Sma I (5975)
Xma I (5973)
Pme I (5761)
AthHMGRt
Pml I (4868)
AThHMGS
Bst BI (3997)
Xba I (3446)
Eco RI (3200)
SceAACT
Nco I (2718)
Xcm I (2320)
Sap I (1919)
Amp
Xmn I (314)
pHKO1
6646 bp

Fig. 4

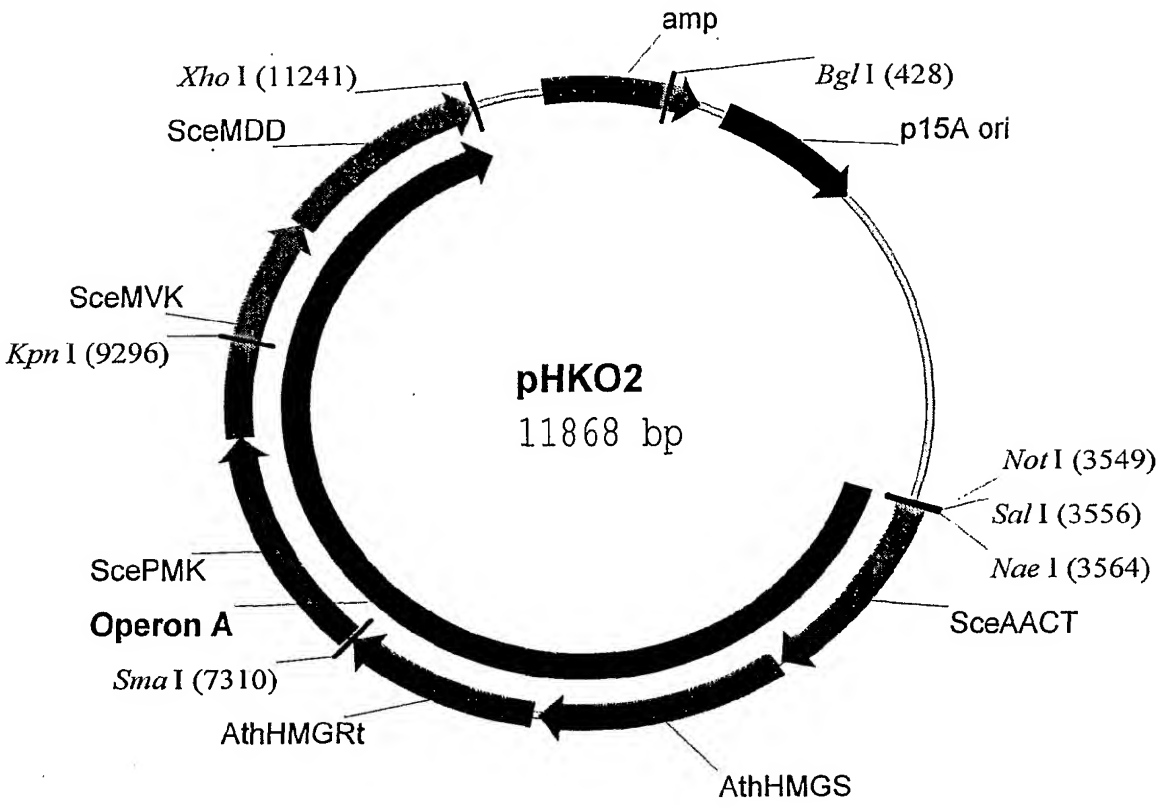

amp
Xho I (11241)
Bgl I (428)
SceMDD
p15A ori
SceMVK
Kpn I (9296)
pHKO2
11868 bp
Not I (3549)
Sal I (3556)
Nae I (3564)
ScePMK
Operon A
SceAACT
Sma I (7310)
AthHMGRt
AthHMGS

Fig. 5

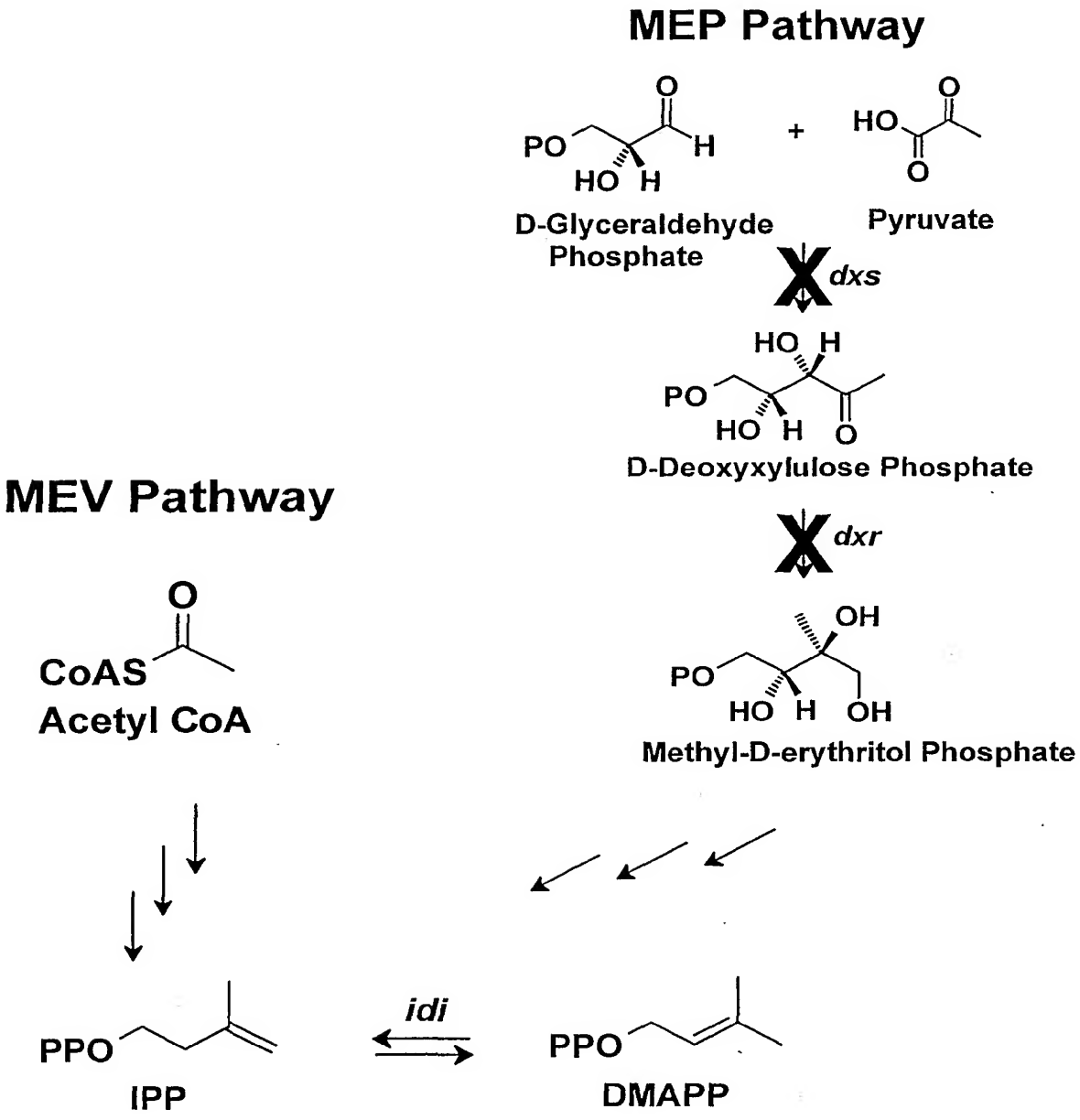

MEP Pathway
D-Glyceraldehyde Phosphate
Pyruvate
dxs
D-Deoxyxylulose Phosphate
dxr
Methyl-D-erythritol Phosphate
MEV Pathway
CoAS
Acetyl CoA
idi
IPP
DMAPP

Fig. 6

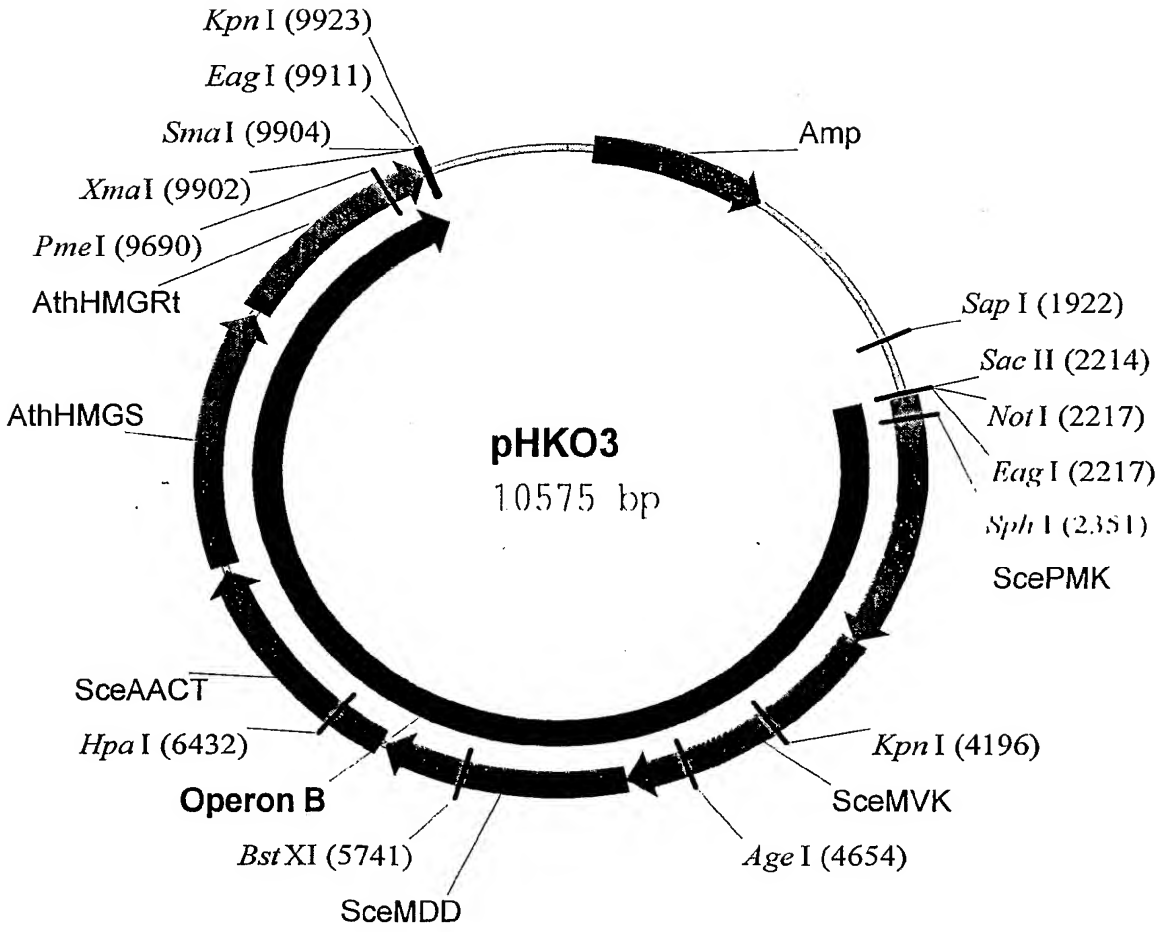

Kpn I (9923)
Eag I (9911)
Sma I (9904)
Xma I (9902)
Pme I (9690)
AthHMGRt
AthHMGS
SceAACT
Hpa I (6432)
Operon B
Bst XI (5741)
SceMDD
Age I (4654)
SceMVK
Kpn I (4196)
ScePMK
Eag I (2217)
Not I (2217)
Sac II (2214)
Sap I (1922)
Amp
pHKO3
10575 bp

Fig. 7

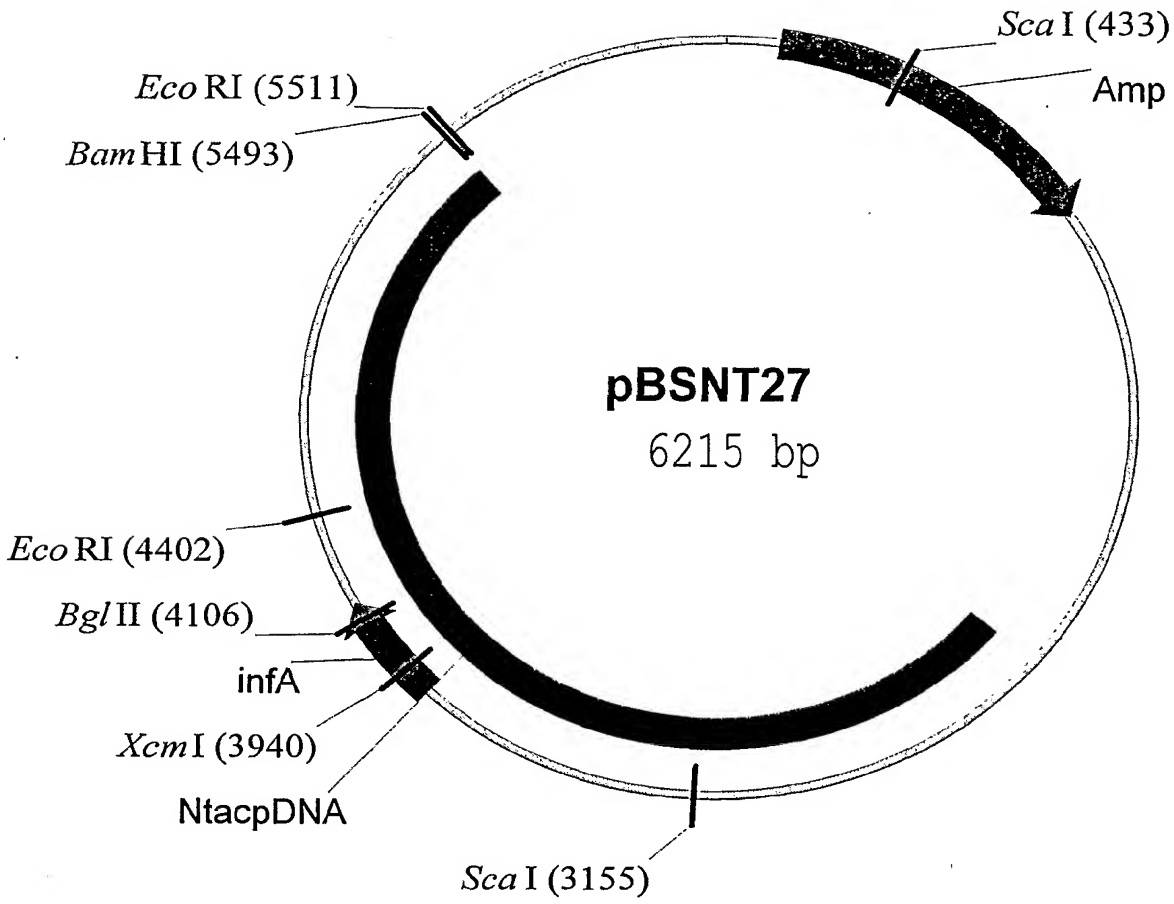

ScaI (433)
Amp
EcoRI (5511)
BamHI (5493)
pBSNT27
6215 bp
EcoRI (4402)
BglII (4106)
infA
XcmI (3940)
NtacpDNA
ScaI (3155)

Fig. 8

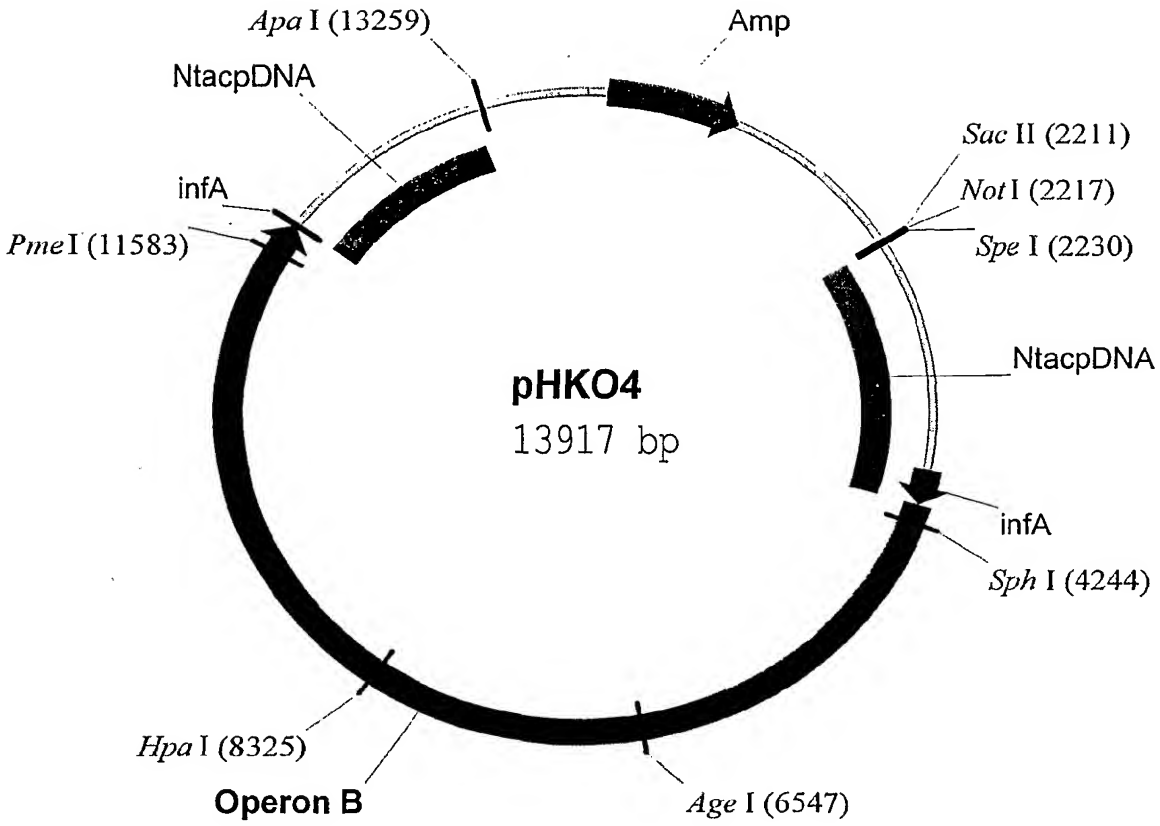

Apa I (13259)
Amp
NtacpDNA
Sac II (2211)
infA
Not I (2217)
Pme I (11583)
Spe I (2230)
NtacpDNA
pHKO4
13917 bp
infA
Sph I (4244)
Hpa I (8325)
Operon B
Age I (6547)

Fig. 9

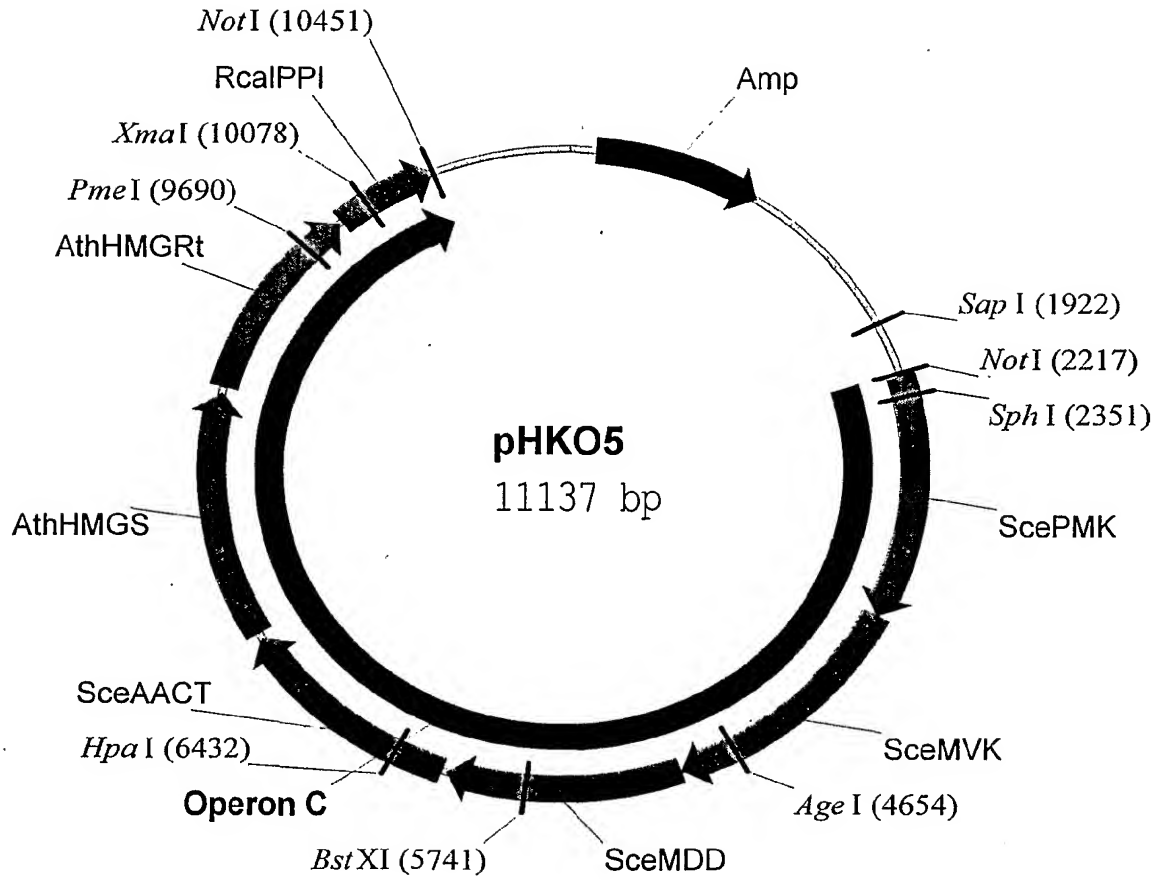

NotI (10451)
RcalPPI
XmaI (10078)
PmeI (9690)
AthHMGRt
Amp
Sap I (1922)
NotI (2217)
Sph I (2351)
pHKO5
11137 bp
ScePMK
AthHMGS
SceAACT
HpaI (6432)
Operon C
SceMVK
AgeI (4654)
BstXI (5741)
SceMDD

Fig. 10

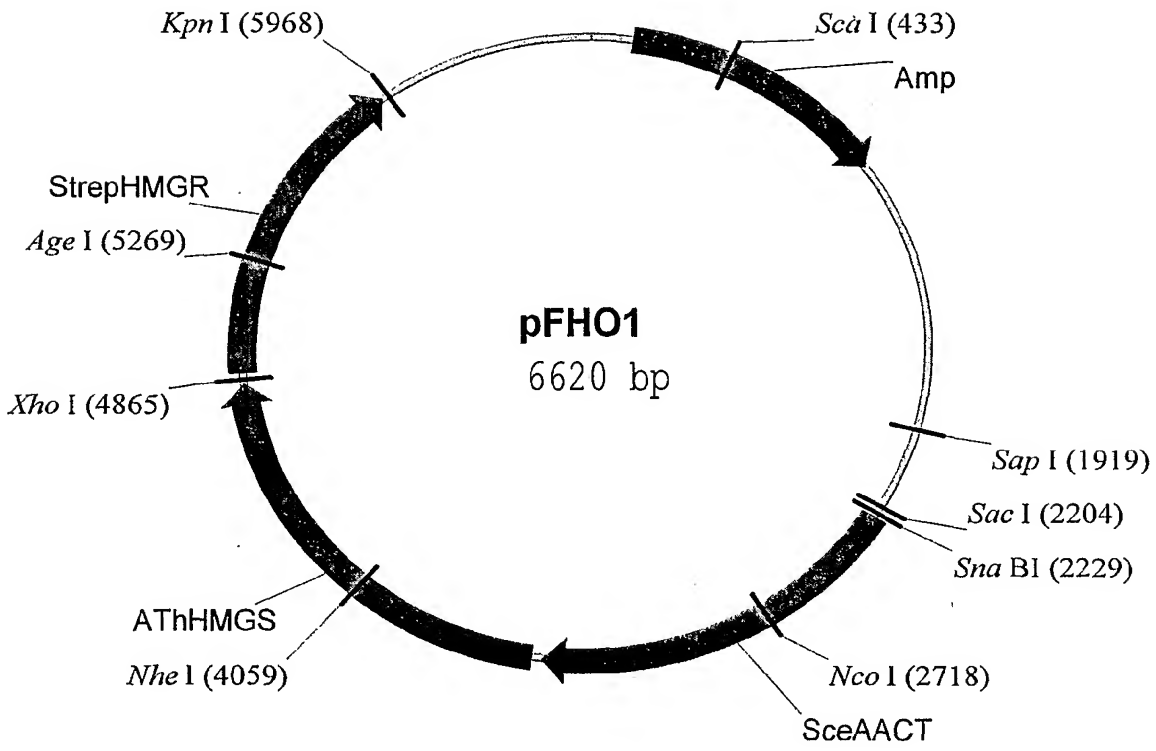

Kpn I (5968)
Sca I (433)
Amp
StrepHMGR
Age I (5269)
pFHO1
6620 bp
Xho I (4865)
Sap I (1919)
Sac I (2204)
Sna BI (2229)
AThHMGS
Nhe I (4059)
Nco I (2718)
SceAACT

Fig. 11

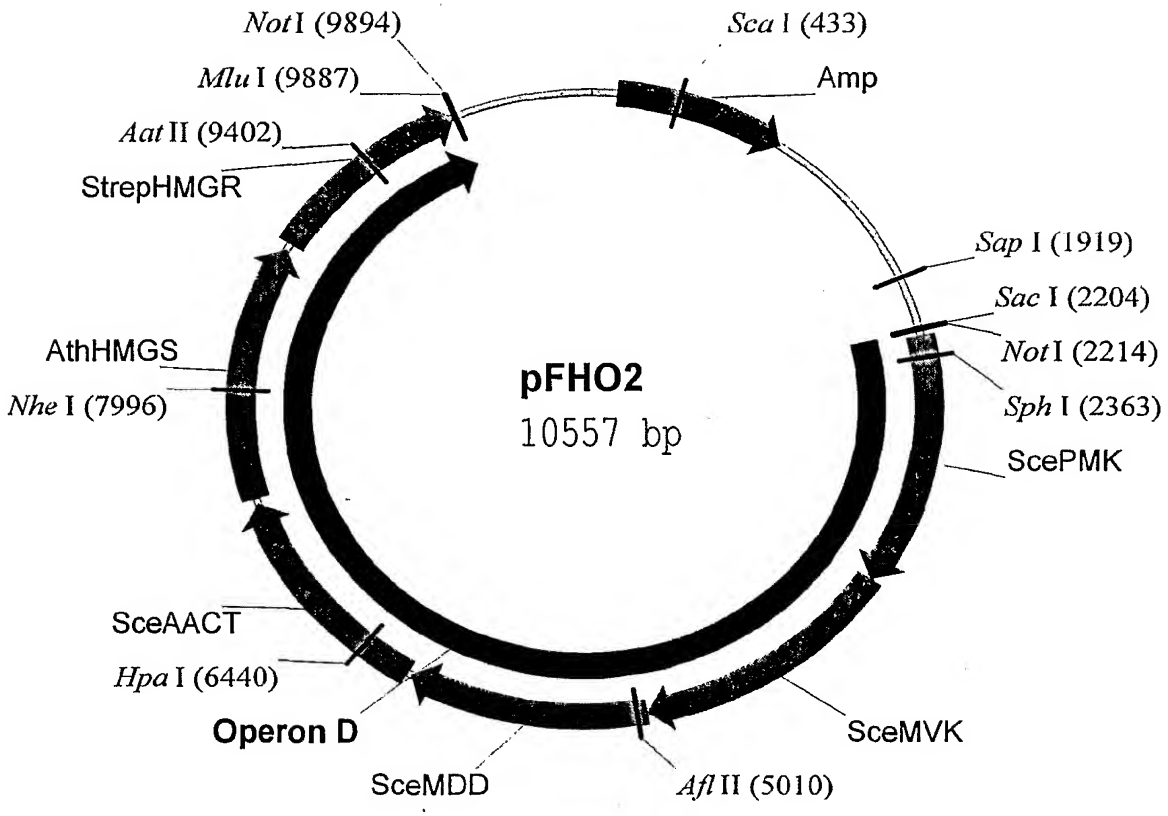

NotI (9894)
Sca I (433)
MluI (9887)
Amp
Aat II (9402)
StrepHMGR
Sap I (1919)
Sac I (2204)
AthHMGS
NotI (2214)
pFHO2
10557 bp
Nhe I (7996)
Sph I (2363)
ScePMK
SceAACT
Hpa I (6440)
Operon D
SceMVK
SceMDD
AflII (5010)

Fig. 12

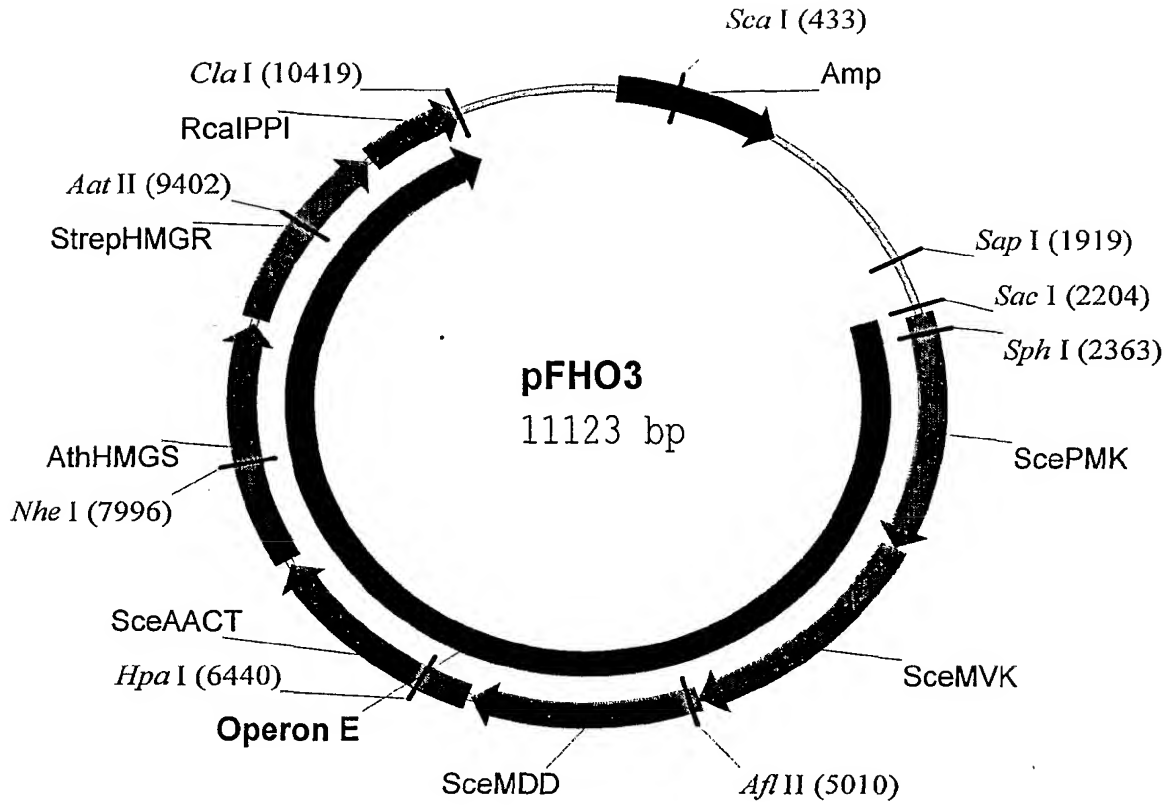

Sca I (433)
Amp
Cla I (10419)
RcaIPPI
Aat II (9402)
StrepHMGR
Sap I (1919)
Sac I (2204)
Sph I (2363)
pFHO3
11123 bp
ScePMK
AthHMGS
Nhe I (7996)
SceAACT
Hpa I (6440)
Operon E
SceMVK
SceMDD
Afl II (5010)

Fig. 13

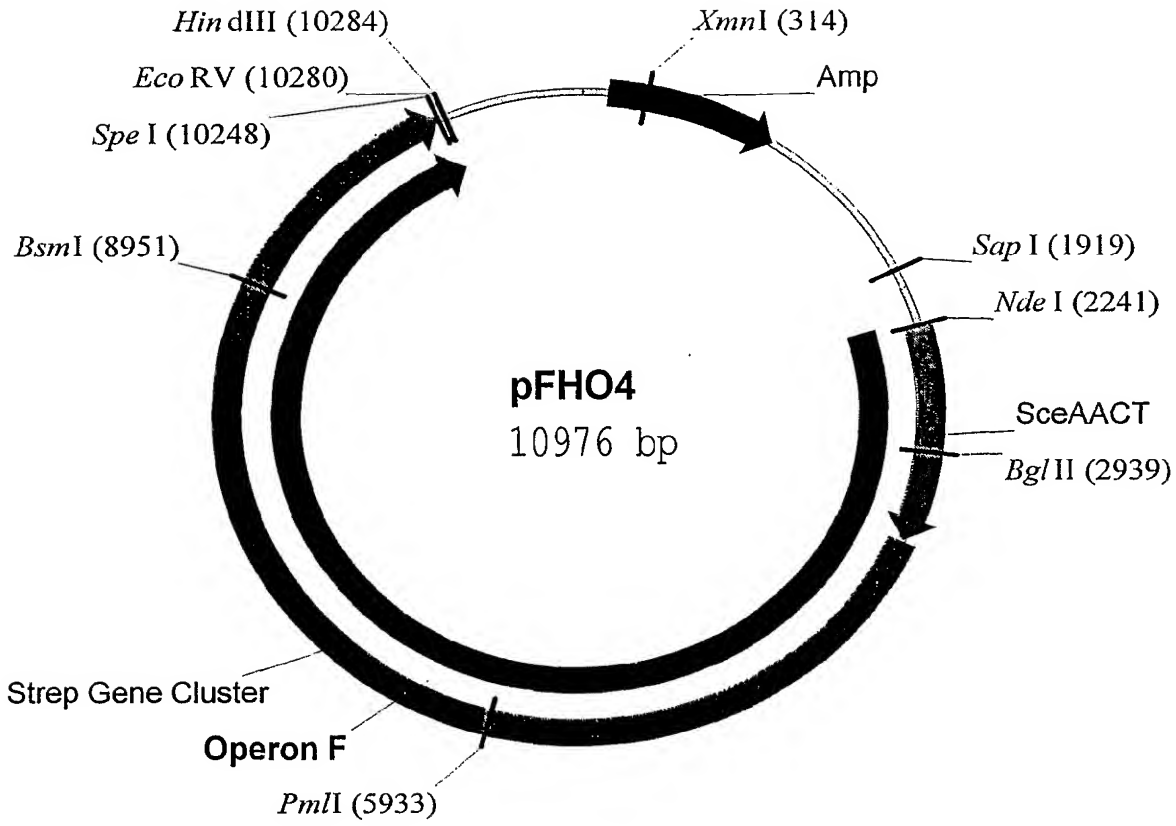

Hin dIII (10284)
Eco RV (10280)
Spe I (10248)
*Xmn*I (314)
Amp
Sap I (1919)
Nde I (2241)
SceAACT
Bgl II (2939)
*Bsm*I (8951)
pFHO4
10976 bp
Strep Gene Cluster
Operon F
*Pml*I (5933)

Fig. 14

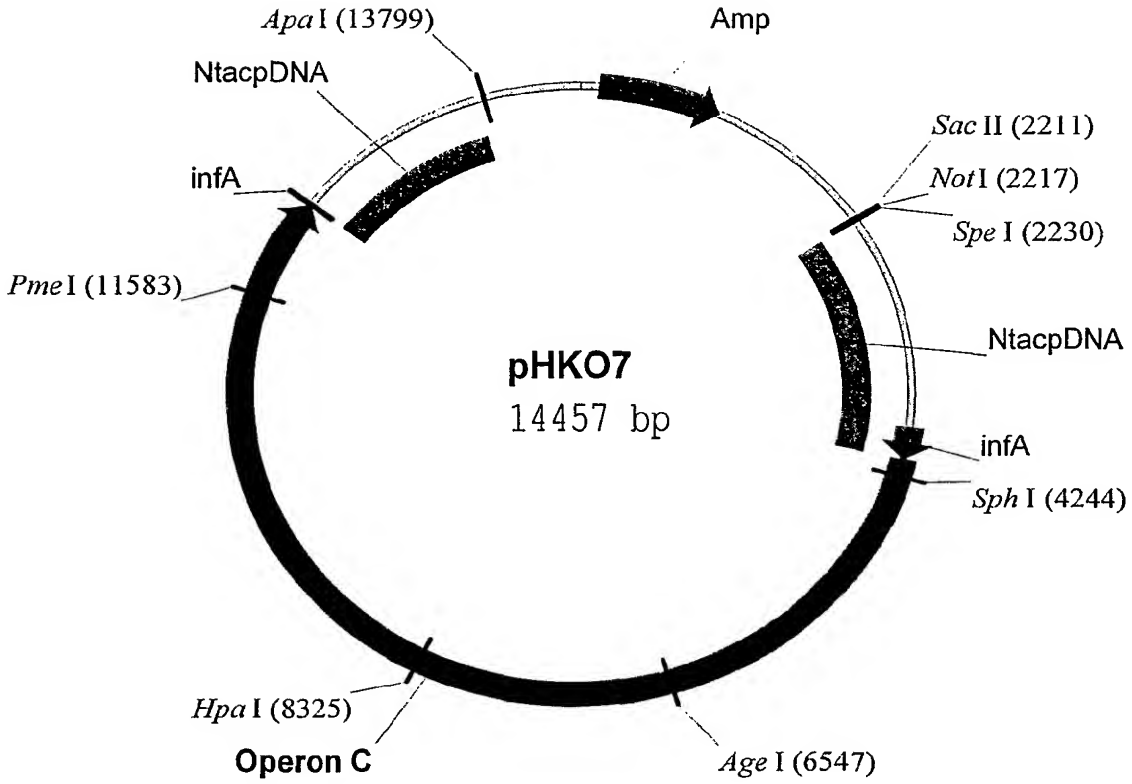

Apa I (13799)
Amp
NtacpDNA
Sac II (2211)
infA
Not I (2217)
Spe I (2230)
Pme I (11583)
NtacpDNA
pHKO7
14457 bp
infA
Sph I (4244)
Hpa I (8325)
Operon C
Age I (6547)

Fig. 15

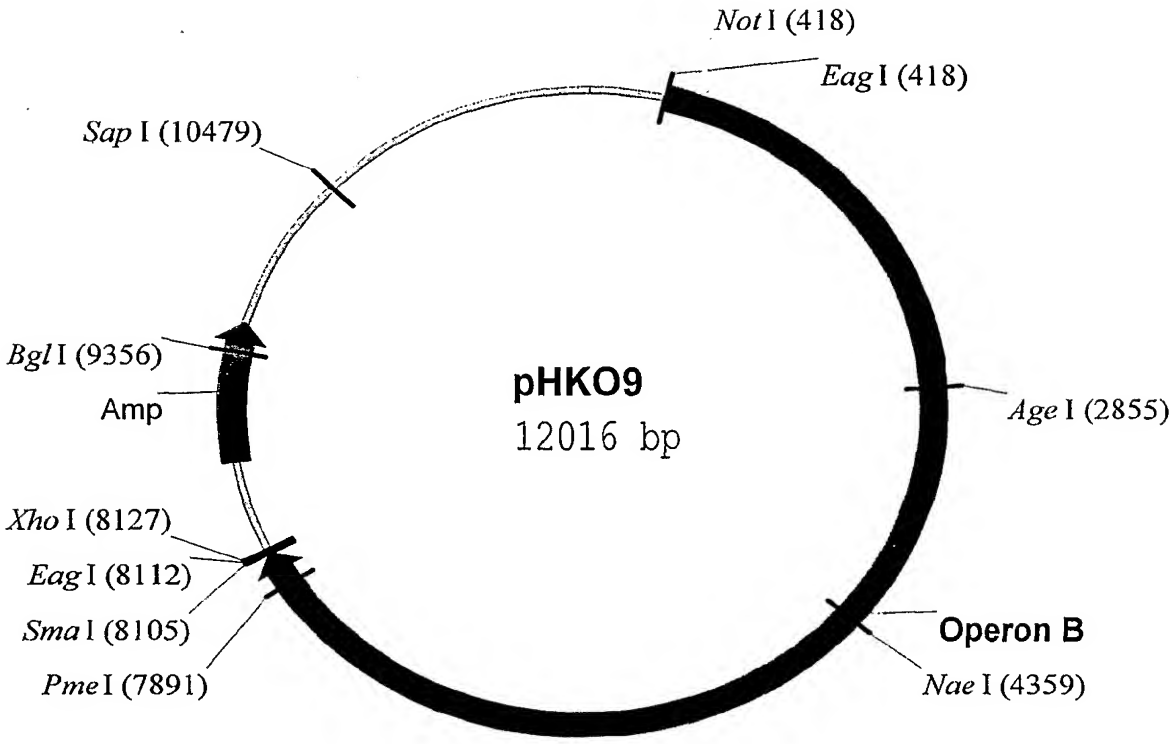

Not I (418)
Eag I (418)
Sap I (10479)
Bgl I (9356)
Amp
pHKO9
12016 bp
Age I (2855)
Xho I (8127)
Eag I (8112)
Sma I (8105)
Pme I (7891)
Operon B
Nae I (4359)

Fig. 16

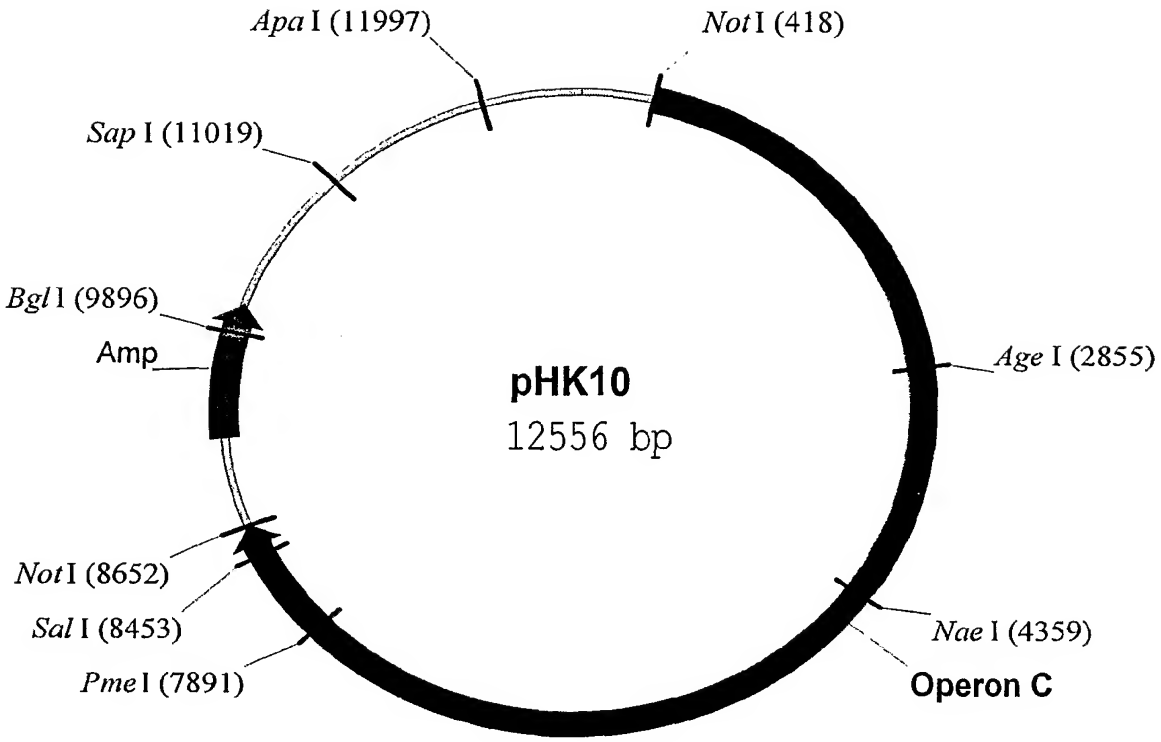
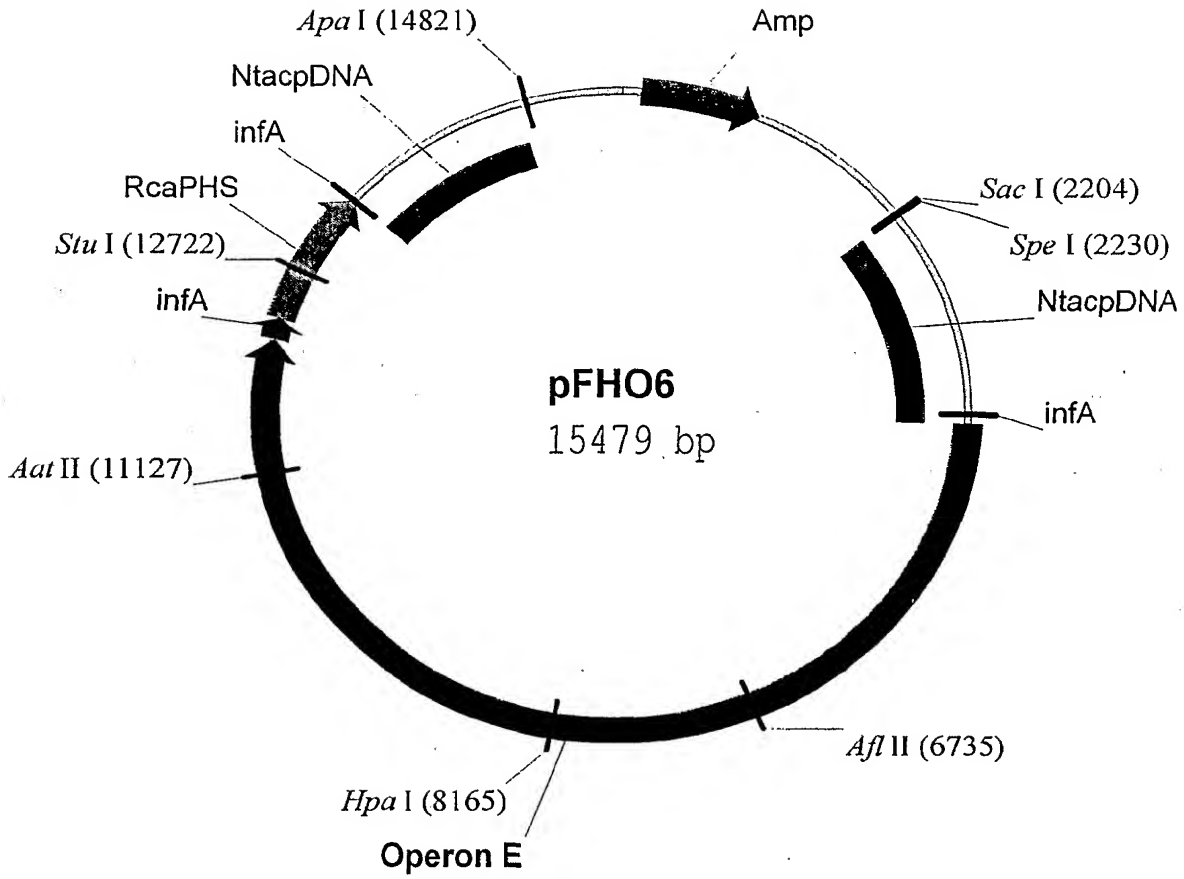

Apa I (11997)
Not I (418)
Sap I (11019)
Bgl I (9896)
Amp
pHK10
12556 bp
Age I (2855)
Not I (8652)
Sal I (8453)
Pme I (7891)
Nae I (4359)
Operon C

Fig. 17


Apa I (14821)
Amp
NtacpDNA
infA
RcaPHS
Sac I (2204)
Stu I (12722)
Spe I (2230)
infA
NtacpDNA
pFHO6
15479 bp
infA
Aat II (11127)
Afl II (6735)
Hpa I (8165)
Operon E

SEQUENCE LISTING

<110> Hahn, Frederick

Kuehnle, Adelheid

<120> Manipulation of genes of the mevalonate and isoprenoid pathways to create novel traits in transgenic organisms

<130> KAS-103XC1

<150> 60/221,703

<151> 2000-07-31

<160> 76

<170> PatentIn version 3.0

<210> 1

<211> 57

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer containing Saccharomyces cerevisiae DNA

<400> 1
ggactagtct gcaggaggag ttttaatgtc attaccgttc ttaacttctg caccggg 57

<210> 2

<211> 96

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer containing S. cerevisiae DNA

<400> 2

ttctcgagct taagagtagc aatatttacc ggagcagtta cactagcagt atatacagtc 60

attaaaactc ctcctgtgaa gtccatggta aattcg 96

<210> 3

<211> 56

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer containing S. cerevisiae DNA

<400> 3
tagcggccgc aggaggagtt catatgtcag agttgagagc cttcagtgcc ccaggg 56

<210> 4

<211> 36

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer containing S. cerevisiae DNA

<400> 4
tttctgcagt ttatcaagat aagtttccgg atcttt 36

<210> 5

<211> 41

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer containing S. cerevisiae DNA

<400> 5
ggaattcatg accgtttaca cagcatccgt taccgcaccc g 41

<210> 6

<211> 45

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer containing S. cerevisiae DNA

<400> 6
ggctcgagtt aaaactcctc ttcctttggt agaccagtct ttgcg 45

<210> 7

<211> 68

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer containing Arabidopsis thaliana DNA

<400> 7
gctctagatg cgcaggaggc acatatggcg aagaacgttg ggattttggc tatggatatc 60

tatttccc 68

<210> 8

<211> 61

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer containing A. thaliana DNA

<400> 8
cgctcgagtc gacggatcct cagtgtccat tggctacaga tccatcttca cctttcttgc 60

c 61

<210> 9

<211> 72

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer containing A. thaliana DNA

<400> 9

ccgctcgagc acgtggaggc acatatgcaa tgctgtgaga tgcctgttgg atacattcag 60

attcctgttg gg 72

<210> 10

<211> 71

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer containing A. thaliana DNA

<400> 10
ggggtacctg cggccggatc ccgggtcatg ttgttgttgt tgtcgttgtc gttgctccag 60

agatgtctcg g 71

<210> 11

<211> 74

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer containing S. cerevisiae DNA

<400> 11
acaacaccgc ggcggccgcg tcgacgccgg cggaggcaca tatgtctcag aacgtttaca 60

ttgtatcgac tgcc 74

<210> 12

<211> 53

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer containing S. cerevisiae DNA

<400> 12
gctctagagg atcctcatat cttttcaatg acaatagagg aagcaccacc acc 53

<210> 13

<211> 65

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide containing S. cerevisiae DNA

<400> 13
gctctagata cgtaggaggc acatatgagt gagcttatac ccgcctgggt tggtgacaga 60

ctggc 65

<210> 14

<211> 61

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide containing A. thaliana and S. cerevisiae DNA

<400> 14
cgctcgagcc cgggggatcc tcagccgcgc aggatcgatc cgaaaatccg gtcaagatgg 60

c 61

<210> 15

<211> 72

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide containing S. cerevisiae DNA

<400> 15
gctctagata cgtaggaggc acatatgagt tcccaacaag agaaaaagga ttatgatgaa 60

gaacaattaa gg 72

<210> 16

<211> 59

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide containing S. cerevisiae DNA

<400> 16
cgctcgagcc cgggggatcc ttagcaacga tgaattaagg tatcttggaa ttttgacgc 59

<210> 17

<211> 6215

<212> DNA

<213> Artificial Sequence

<220>

<221> misc_feature

<222> ()..()

<223> Vector pBSNT27 containing Nicotiana tabacum DNA

<400> 17
gcacttttcg gggaaatgtg cgcggaaccc ctatttgttt atttttctaa atacattcaa 60

atatgtatcc gctcatgaga caataaccct gataaatgct tcaataatat tgaaaaagga 120

agagtatgag tattcaacat ttccgtgtcg cccttattcc ctttttgcg gcattttgcc 180

ttcctgtttt tgctcaccca gaaacgctgg tgaaagtaaa agatgctgaa gatcagttgg 240

gtgcacgagt gggttacatc gaactggatc tcaacagcgg taagatcctt gagagttttc 300

gccccgaaga acgttttcca atgatgagca cttttaaagt tctgctatgt ggcgcggtat 360

tatcccgtat tgacgccggg caagagcaac tcggtcgccg catacactat tctcagaatg 420

acttggttga gtactcacca gtcacagaaa agcatcttac ggatggcatg acagtaagag 480

aattatgcag tgctgccata accatgagtg ataacactgc ggccaactta cttctgacaa 540

cgatcggagg accgaaggag ctaaccgctt ttttgcacaa catgggggat catgtaactc 600

gccttgatcg ttgggaaccg gagctgaatg aagccatacc aaacgacgag cgtgacacca 660

cgatgcctgt agcaatggca acaacgttgc gcaaactatt aactggcgaa ctacttactc 720

tagcttcccg gcaacaatta atagactgga tggaggcgga taaagttgca ggaccacttc 780

tgcgctcggc ccttccggct ggctggttta ttgctgataa atctggagcc ggtgagcgtg 840

ggtctcgcgg tatcattgca gcactggggc cagatggtaa gccctcccgt atcgtagtta 900

tctacacgac ggggagtcag gcaactatgg atgaacgaaa tagacagatc gctgagatag 960

gtgcctcact gattaagcat tggtaactgt cagaccaagt ttactcatat atactttaga 1020

ttgatttaaa acttcatttt taatttaaaa ggatctaggt gaagatcctt tttgataatc 1080
tcatgaccaa aatcccttaa cgtgagtttt cgttccactg agcgtcagac cccgtagaaa 1140
agatcaaagg atcttcttga gatccttttt ttctgcgcgt aatctgctgc ttgcaaacaa 1200
aaaaaccacc gctaccagcg gtggtttgtt tgccggatca agagctacca actcttttc 1260
cgaaggtaac tggcttcagc agagcgcaga taccaaatac tgtccttcta gtgtagccgt 1320
agttaggcca ccacttcaag aactctgtag caccgcctac atacctcgct ctgctaatcc 1380
tgttaccagt ggctgctgcc agtggcgata agtcgtgtct taccgggttg gactcaagac 1440
gatagttacc ggataaggcg cagcggtcgg gctgaacggg gggttcgtgc acacagccca 1500
gcttggagcg aacgacctac accgaactga gatacctaca gcgtgagcta tgagaaagcg 1560
ccacgcttcc cgaagggaga aaggcggaca ggtatccggt aagcggcagg gtcggaacag 1620
gagagcgcac gagggagctt ccagggggaa acgcctggta tctttatagt cctgtcgggt 1680
ttcgccacct ctgacttgag cgtcgatttt tgtgatgctc gtcaggggggg cggagcctat 1740
ggaaaaacgc cagcaacgcg gccttttttac ggttcctggc cttttgctgg ccttttgctc 1800
acatgttctt tcctgcgtta tcccctgatt ctgtggataa ccgtattacc gcctttgagt 1860
gagctgatac cgctcgccgc agccgaacga ccgagcgcag cgagtcagtg agcgaggaag 1920
cggaagagcg cccaatacgc aaaccgcctc tccccgcgcg ttggccgatt cattaatgca 1980
gctggcacga caggtttccc gactggaaag cgggcagtga gcgcaacgca attaatgtga 2040
gttagctcac tcattaggca ccccaggctt tacactttat gcttccggct cgtatgttgt 2100
gtggaattgt gagcggataa caatttcaca caggaaacag ctatgaccat gattacgcca 2160
agctcgaaat taaccctcac taaagggaac aaaagctgga gctccaccgc ggtggcggcc 2220
gctctagaac tagtggatct tcttggctgt tattcaaaag gtccaacaat gtatatatat 2280
tggacatttt gaggcaatta tagatcctgg aaggcaattc tgattggtca ataaaaatcg 2340
atttcaatgc tatttttttt ttgtttttta tgagtttagc caatttatca tgaaaggtaa 2400
aaggggataa aggaaccgtg tgttgattgt cctgtaaata taagttgtct tcctccatat 2460
gtaaaaaggg aataaataaa tcaattaaat ttcgggatgc ttcatgaagt gcttctttcg 2520
gagttaaact tccgtttgtc catatttcga gaaaaagtat ctcttgtttt tcattcccat 2580
tcccataaga atgaatacta tgattcgcgt ttcgaacagg catgaataca gcatctatag 2640
gataacttcc atcttgaaag ttatgtggcg tttttataag atatccacga tttctctcta 2700
tttgtaatcc aatacaaaaa tcaattggtt ccgttaaact ggctatatgt tgtgtattat 2760
caacgatttc tacataaggc ggcaagatga tatcttgggc agttacagat ccaggaccct 2820
tgacacaaat agatgcgtca gaagttccat atagattact tcttaatata atttctttca 2880
aattcattaa aatttcatgt accgattctt gaatgcccgt tatggtagaa tattcatgtg 2940

ggactttctc agattttaca cgtgtgatac atgttccttc tatttctcca agtaaagctc 3000
ttcgcatcgc aatgcctatt gtgtcggctt ggcctttcat aagtggagac agaataaagc 3060
gtccataata aaggcgttta ctgtctgttc ttgattcaac acacttccac tgtagtgtcc 3120
gagtagatac tgttactttc tctcgaacca tagtactatt atttgattag atcatcgaat 3180
cttttatttc tcttgagatt tcttcaatgt tcagttctac acacgtcttt ttttcggagg 3240
tctacagcca ttatgtggca taggagttac atcccgtacg aaagttaata gtataccact 3300
tcgacgaata gctcgtaatg ctgcatctct tccgagaccg ggacctttta tcatgacttc 3360
tgctcgttgc ataccttgat ccactactgt acggatagcg tttgctgctg cggtttgagc 3420
agcaaacggt gttcctcttc tcgtaccttt gaatccagaa gtaccggcgg aggaccaaga 3480
aactactcga ccccgtacat ctgtaacagt gacaatggta ttattgaaac ttgcttgaac 3540
atgaataact ccctttggta ttctacgtgc acccttacgt gaaccaatac gtccattcct 3600
acgcgaacta attttcggta tagcttttgc catattttat catctcgtaa atatgagtca 3660
gagatatatg gatatatcca tttcatgtca aaacagattc tttatttgta catcggctct 3720
tctggcaagt ctgattatcc ctgtctttgt ttatgtctcg ggttggaaca aattactata 3780
attcgtcccc gcctacggat tagtcgacat ttttcacaaa ttttacgaac ggaagctctt 3840
attttcatat ttctcattcc ttaccttaat tctgaatcta tttcttggaa gaaaataagt 3900
ttcttgaaat ttttcatctc gaattgtatt cccacgaaag gaatggtgaa gttgaaaaac 3960
gaatccttca aatctttgtt gtggagtcga taaattatac gccctttggt tgaatcataa 4020
ggacttactt caattttgac tctatctcct ggcagtatcc gtataaaact atgccggatc 4080
tttcctgaaa cataatttat aatcagatct aaacaaaccc ggaacagacc gttgggaagc 4140
gattcagtaa ttaaagcttc atgactcctt tttggttctt aaagtccctt tgaggtatca 4200
actaataaga aagatattag acaacccccc ttttttcttt ttcacaaata ggaagtttcg 4260
aatccaattt ggatattaaa aggattacca gatataacac aaaatctctc cacctattcc 4320
ttctagtcga gcctctcggt ctgtcattat acctcgagaa gtagaaagaa ttacaatccc 4380
cattccacct aaaattcgcg gaattcgttg ataattagaa tagattcgta gaccaggtcg 4440
actgattcgt tttaaattta aaatatttct atagggtctt ttcctattcc ttctatgtcg 4500
cagggttaaa accaaaaaat atttgttttt ttctcgatgt tttctcacgt tttcgataaa 4560
accttctcgt aaaagtattt gaacaatatt ttcggtaata ttagtagatg ctattcgaac 4620
caccctttt cgatccatat cagcatttcg tatagaagtt attatctcag caatagtgtc 4680
cctacccatg atgaactaaa attattgggg cctccaaatt tgatataatc aacgtgtttt 4740
ttacttattt tttttttgaa tatgatatga attattaaag atatatgcgt gagacacaat 4800
ctactaatta atctatttct ttcaaatacc ccactagaaa cagatcacaa tttcatttta 4860

taatacctcg ggagctaatg aaactatttt agtaaaattt aattctctca attcccgggc 4920
gattgcacca aaaattcgag ttccttttga tttccttcct tcttgatcaa taacaactgc 4980
agcattgtca tcatatcgta ttatcatccc gttgtcacgt ttgagttctt tacaggtccg 5040
cacaattaca gctctgacta cttctgatct ttctaggggc atatttggta cggcttcttt 5100
gatcacagca acaataacgt caccaatatg agcatatcga cgattgctag ctcctatgat 5160
tcgaatacac atcaattctc gagccccgct gttatccgct acatttaaat gggtctgagg 5220
ttgaatcatt tttttaatcc gttctttgaa tgcaaagggc gaagaaaaaa aagaaatatt 5280
tttgtccaaa aaaaaagaaa catgcggttt cgtttcatat ctaagagccc tttccgcatt 5340
tttttctatt acattacgaa ataatgaatt gagttcgtat aggcatttta gatgctgcta 5400
gtgaaatagc ccttctggct atattttctg ttactccacc catttcataa agtattcgac 5460
ccggtttaac aacagctacc caatattcag gggatccccc gggctgcagg aattcgatat 5520
caagcttatc gataccgtcg acctcgaggg ggggcccggt acccaattcg ccctatagtg 5580
agtcgtatta caattcactg gccgtcgttt tacaacgtcg tgactgggaa aaccctggcg 5640
ttacccaact taatcgcctt gcagcacatc ccccttcgc cagctggcgt aatagcgaag 5700
aggcccgcac cgatcgccct tcccaacagt tgcgcagcct gaatggcgaa tgggacgcgc 5760
cctgtagcgg cgcattaagc gcggcgggtg tggtggttac gcgcagcgtg accgctacac 5820
ttgccagcgc cctagcgccc gctcctttcg ctttcttccc ttcctttctc gccacgttcg 5880
ccggctttcc ccgtcaagct ctaaatcggg ggctcccttt agggttccga tttagtgctt 5940
tacggcacct cgaccccaaa aaacttgatt agggtgatgg ttcacgtagt gggccatcgc 6000
cctgatagac ggtttttcgc cctttgacgt tggagtccac gttctttaat agtggactct 6060
tgttccaaac tggaacaaca ctcaacccta tctcggtcta ttcttttgat ttataaggga 6120
ttttgccgat ttcggcctat tggttaaaaa atgagctgat ttaacaaaaa tttaacgcga 6180
attttaacaa aatattaacg cttacaattt aggtg 6215

<210> 18

<211> 1332

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide containing N. tabacum and S. cerevisiae DNA

<400> 18

atgtcattac cgttcttaac ttctgcaccg ggaaaggtta ttatttttgg tgaacactct 60
gctgtgtaca acaagcctgc cgtcgctgct agtgtgtctg cgttgagaac ctacctgcta 120
ataagcgagt catctgcacc agatactatt gaattggact tcccggacat tagctttaat 180
cataagtggt ccatcaatga tttcaatgcc atcaccgagg atcaagtaaa ctcccaaaaa 240
ttggccaagg ctcaacaagc caccgatggc ttgtctcagg aactcgttag tcttttggat 300
ccgttgttag ctcaactatc cgaatccttc cactaccatg cagcgttttg tttcctgtat 360
atgtttgttt gcctatgccc ccatgccaag aatattaagt tttctttaaa gtctacttta 420
cccatcggtg ctgggttggg ctcaagcgcc tctatttctg tatcactggc cttagctatg 480
gcctacttgg gggggttaat aggatctaat gacttggaaa agctgtcaga aaacgataag 540
catatagtga atcaatgggc cttcataggt gaaaagtgta ttcacggtac cccttcagga 600
atagataacg ctgtggccac ttatggtaat gccctgctat ttgaaaaaga ctcacataat 660
ggaacaataa acacaaacaa ttttaagttc ttagatgatt tcccagccat tccaatgatc 720
ctaacctata ctagaattcc aaggtctaca aaagatcttg ttgctcgcgt tcgtgtgttg 780
gtcaccgaga aatttcctga agttatgaag ccaattctag atgccatggg tgaatgtgcc 840
ctacaaggct tagagatcat gactaagtta agtaaatgta aaggcaccga tgacgaggct 900
gtagaaacta ataatgaact gtatgaacaa ctattggaat tgataagaat aaatcatgga 960
ctgcttgtct caatcggtgt ttctcatcct ggattagaac ttattaaaaa tctgagcgat 1020
gatttgagaa ttggctccac aaaacttacc ggtgctggtg gcggcggttg ctctttgact 1080
ttgttacgaa gagacattac tcaagagcaa attgacagct tcaaaaagaa attgcaagat 1140
gattttagtt acgagacatt tgaaacagac ttgggtggga ctggctgctg tttgttaagc 1200
gcaaaaaatt tgaataaaga tcttaaaatc aaatccctag tattccaatt atttgaaaat 1260
aaaactacca caaagcaaca aattgacgat ctattattgc caggaaacac gaatttacca 1320
tggacttcat aa 1332

<210> 19

<211> 1191

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide containing N. tabacum and A. thaliana DNA

<400> 19
atgaccgttt acacagcatc cgttaccgca cccgtcaaca tcgcaaccct taagtattgg 60

gggaaaaggg acacgaagtt gaatctgccc accaattcgt ccatatcagt gactttatcg 120

caagatgacc tcagaacgtt gacctctgcg gctactgcac ctgagtttga acgcgacact 180

ttgtggttaa atggagaacc acacagcatc gacaatgaaa gaactcaaaa ttgtctgcgc 240

gacctacgcc aattaagaaa ggaaatggaa tcgaaggacg cctcattgcc cacattatct 300

caatggaaac tccacattgt ctccgaaaat aactttccta cagcagctgg tttagcttcc 360

tccgctgctg gctttgctgc attggtctct gcaattgcta agttatacca attaccacag 420

tcaacttcag aaatatctag aatagcaaga aaggggtctg gttcagcttg tagatcgttg 480

tttggcggat acgtggcctg ggaaatggga aaagctgaag atggtcatga ttccatggca 540

gtacaaatcg cagacagctc tgactggcct cagatgaaag cttgtgtcct agttgtcagc 600

gatattaaaa aggatgtgag ttccactcag ggtatgcaat tgaccgtggc aacctccgaa 660

ctatttaaag aaagaattga acatgtcgta ccaaagagat ttgaagtcat gcgtaaagcc 720

attgttgaaa aagatttcgc cacctttgca aaggaaacaa tgatggattc caactctttc 780

catgccacat gtttggactc tttccctcca atattctaca tgaatgacac ttccaagcgt 840

atcatcagtt ggtgccacac cattaatcag ttttacggag aaacaatcgt tgcatacacg 900

tttgatgcag gtccaaatgc tgtgttgtac tacttagctg aaaatgagtc gaaactcttt 960

gcatttatct ataaattgtt tggctctgtt cctggatggg acaagaaatt tactactgag 1020

cagcttgagg ctttcaacca tcaatttgaa tcatctaact ttactgcacg tgaattggat 1080

cttgagttgc aaaaggatgt tgccagagtg attttaactc aagtcggttc aggcccacaa 1140

gaaacaaacg aatctttgat tgacgcaaag actggtctac caaaggaata a 1191

<210> 20

<211> 1197

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer containing Rhodobacter capsulatus DNA

<400> 20

atgtctcaga acgtttacat tgtatcgact gccagaaccc caattggttc attccagggt 60

tctctatcct ccaagacagc agtggaattg ggtgctgttg ctttaaaagg cgccttggct 120

aaggttccag aattggatgc atccaaggat tttgacgaaa ttatttttgg taacgttctt 180

tctgccaatt tgggccaagc tccggccaga caagttgctt tggctgccgg tttgagtaat 240

catatcgttg caagcacagt taacaaggtc tgtgcatccg ctatgaaggc aatcattttg 300

ggtgctcaat ccatcaaatg tggtaatgct gatgttgtcg tagctggtgg ttgtgaatct 360

atgactaacg caccatacta catgccagca gcccgtgcgg gtgccaaatt tggccaaact 420

gttcttgttg atggtgtcga aagagatggg ttgaacgatg cgtacgatgg tctagccatg 480

ggtgtacacg cagaaaagtg tgcccgtgat tgggatatta ctagagaaca acaagacaat 540

tttgccatcg aatcctacca aaaatctcaa aaatctcaaa aggaaggtaa attcgacaat 600

gaaattgtac ctgttaccat taagggattt agaggtaagc ctgatactca agtcacgaag 660

gacgaggaac ctgctagatt acacgttgaa aaattgagat ctgcaaggac tgttttccaa 720

aaagaaaacg gtactgttac tgccgctaac gcttctccaa tcaacgatgg tgctgcagcc 780

gtcatcttgg tttccgaaaa agttttgaag gaaaagaatt tgaagccttt ggctattatc 840

aaaggttggg gtgaggccgc tcatcaacca gctgatttta catgggctcc atctcttgca 900

gttccaaagg ctttgaaaca tgctggcatc gaagacatca attctgttga ttactttgaa 960

ttcaatgaag ccttttcggt tgtcggtttg gtgaacacta agattttgaa gctagaccca 1020

tctaaggtta atgtatatgg tggtgctgtt gctctaggtc acccattggg ttgttctggt 1080

gctagagtgg ttgttacact gctatccatc ttacagcaag aaggaggtaa gatcggtgtt 1140

gccgccattt gtaatggtgg tggtggtgct tcctctattg tcattgaaaa gatatga 1197

<210> 21

<211> 1386

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer containing R. capsulatus DNA

<400> 21

atggcgaaga acgttgggat tttggctatg gatatctatt tccctcccac ctgtgttcaa 60

caggaagctt tggaagcaca tgatggagca agtaaaggga aatacactat tggacttggc 120

caagattgtt tagctttttg cactgagctt gaagatgtta tctctatgag tttcaatgcg 180

gtgacatcac tttttgagaa gtataagatt gaccctaacc aaatcgggcg tcttgaagta 240

ggaagtgaga ctgttattga caaaagcaag tccatcaaga ccttcttgat gcagctcttt 300

gagaaatgtg gaaacactga tgtcgaaggt gttgactcga ccaatgcttg ctatggtgga 360

actgcagctt tgttaaactg tgtcaattgg gttgagagta actcttggga tggacgttat 420

ggcctcgtca tttgtactga cagcgcggtt tatgcagaag gacccgcaag gcccactgga 480

ggagctgcag cgattgctat gttgatagga cctgatgctc ctatcgtttt cgaaagcaaa 540

ttgagagcaa gccacatggc tcatgtctat gacttttaca agcccaatct tgctagcgag 600

tacccggttg ttgatggtaa gctttcacag acttgctacc tcatggctct tgactcctgc 660

tataaacatt tatgcaacaa gttcgagaag atcgagggca aagagttctc cataaatgat 720

gctgattaca ttgttttcca ttctccatac aataaacttg tacagaaaag ctttgctcgt 780

ctcttgtaca acgacttctt gagaaacgca agctccattg acgaggctgc caaagaaaag 840

ttcacccctt attcatcttt gacccttgac gagagttacc aaagccgtga tcttgaaaag 900

gtgtcacaac aaatttcgaa accgttttat gatgctaaag tgcaaccaac gactttaata 960

ccaaaggaag tcggtaacat gtacactgct tctctctacg ctgcatttgc ttccctcatc 1020

cacaataaac acaatgattt ggcgggaaag cgggtggtta tgttctctta tggaagtggc 1080

tccaccgcaa caatgttctc attacgcctc aacgacaata agcctccttt cagcatttca 1140

aacattgcat ctgtaatgga tgttggcggt aaattgaaag ctagacatga gtatgcacct 1200

gagaagtttg tggagacaat gaagctaatg gaacataggt atggagcaaa ggactttgtg 1260

acaaccaagg agggtattat agatcttttg gcaccgggaa cttattatct gaaagaggtt 1320

gattccttgt accggagatt ctatggcaag aaaggtgaag atggatctgt agccaatgga 1380

cactga 1386

<210> 22

<211> 1779

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer containing Schizosaccharomyces pombe DNA

<400> 22

atggatctcc gtcggaggcc tcctaaacca ccggttacca acaacaacaa ctccaacgga 60

tctttccgtt cttatcagcc tcgcacttcc gatgacgatc atcgtcgccg ggctacaaca 120

attgctcctc caccgaaagc atccgacgcg cttcctcttc cgttatatct cacaaacgcc 180

gttttcttca cgctcttctt ctccgtcgcg tattacctcc tccaccggtg gcgtgacaag 240

atccgttaca atacgcctct tcacgtcgtc actatcacag aactcggcgc cattattgct 300

ctcatcgctt cgtttatcta tctcctaggg ttttttggta ttgactttgt tcagtcattt 360

atctcacgtg cctctggtga tgcttgggat ctcgccgata cgatcgatga tgatgaccac 420

cgccttgtca cgtgctctcc accgactccg atcgtttccg ttgctaaatt acctaatccg 480

gaacctattg ttaccgaatc gcttcctgag gaagacgagg agattgtgaa atcggttatc 540

gacggagtta ttccatcgta ctcgcttgaa tctcgtctcg gtgattgcaa aagagcggcg 600

tcgattcgtc gtgaggcgtt gcagagagtc accgggagat cgattgaagg gttaccgttg 660
gatggatttg attatgaatc gattttgggg caatgctgtg agatgcctgt tggatacatt 720
cagattcctg ttgggattgc tggtccattg ttgcttgatg gttatgagta ctctgttcct 780
atggctacaa ccgaaggttg tttggttgct agcactaaca gaggctgcaa ggctatgttt 840
atctctggtg gcgccaccag taccgttctt aaggacggta tgacccgagc acctgttgtt 900
cggttcgctt cggcgagacg agcttcggag cttaagtttt tcttggagaa tccagagaac 960
tttgatactt tggcagtagt cttcaacagg tcgagtagat ttgcaagact gcaaagtgtt 1020
aaatgcacaa tcgcggggaa gaatgcttat gtaaggttct gttgtagtac tggtgatgct 1080
atggggatga atatggtttc taaaggtgtg cagaatgttc ttgagtatct taccgatgat 1140
ttccctgaca tggatgtgat tggaatctct ggtaacttct gttcggacaa gaaacctgct 1200
gctgtgaact ggattgaggg acgtggtaaa tcagttgttt gcgaggctgt aatcagagga 1260
gagatcgtga acaaggtctt gaaaacgagc gtggctgctt tagtcgagct caacatgctc 1320
aagaacctag ctggctctgc tgttgcaggc tctctaggtg gattcaacgc tcatgccagt 1380
aacatagtgt ctgctgtatt catagctact ggccaagatc cagctcaaaa cgtggagagt 1440
tctcaatgca tcaccatgat ggaagctatt aatgacggca aagatatcca tatctcagtc 1500
actatgccat ctatcgaggt ggggacagtg ggaggaggaa cacagcttgc atctcaatca 1560
gcgtgtttaa acctgctcgg agttaaagga gcaagcacag agtcgccggg aatgaacgca 1620
aggaggctag cgacgatcgt agccggagca gttttagctg gagagttatc tttaatgtca 1680
gcaattgcag ctggacagct tgtgagaagt cacatgaaat acaatagatc cagccgagac 1740
atctctggag caacgacaac gacaacaaca acaacatga 1779

<210> 23
<211> 684
<212> DNA
<213> Artificial Sequence
<220>
<223> PCR primer containing S. pombe DNA

<400> 23
atgagttccc aacaagagaa aaaggattat gatgaagaac aattaaggtt gatggaagaa 60
gtttgtatcg ttgtagatga aaatgatgtc cctttaagat atggaacgaa aaaggagtgt 120
catttgatgg aaaatataaa taaaggtctt ttgcatagag cattctctat gttcatcttt 180
gatgagcaaa atcgcctttt acttcagcag cgtgcagaag agaaaattac atttccatcc 240

ttatggacga atacatgttg ctcccaccca ttggatgttg ctggtgaacg tggtaatact 300

ttacctgaag ctgttgaagg tgttaagaat gcagctcaac gcaagctgtt ccatgaattg 360

ggtattcaag ccaagtatat tcccaaagac aaatttcagt ttcttacacg aatccattac 420

cttgctccta gtactggtgc ttggggagag catgaaattg actacattct tttcttcaaa 480

ggtaaagttg agctggatat caatcccaat gaagttcaag cctataagta tgttactatg 540

gaagagttaa aagagatgtt ttccgatcct caatatggat tcacaccatg gttcaaactt 600

atttgtgagc attttatgtt taaatggtgg caggatgtag atcatgcgtc aaaattccaa 660

gataccttaa ttcatcgttg ctaa 684

<210> 24

<211> 531

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer containing Streptomyces sp CL190 DNA

<400> 24

atgagtgagc ttatacccgc ctgggttggt gacagactgg ctccggtgga caagttggag 60

gtgcatttga aagggctccg ccacaaggcg gtgtctgttt tcgtcatgga tggcgaaaac 120

gtgctgatcc agcgccgctc ggaggagaaa tatcactctc ccgggctttg ggcgaacacc 180

tgctgcaccc atccgggctg gaccgaacgc cccgaggaat gcgcggtgcg gcggctgcgc 240

gaggagctgg ggatcaccgg gctttatccc gcccatgccg accggctgga atatcgcgcc 300

gatgtcggcg gcggcatgat cgagcatgag gtggtcgaca tctatctggc ctatgccaaa 360

ccgcatatgc ggatcacccc cgatccgcgc gaagtggccg aggtgcgctg gatcggcctt 420

tacgatctgg cggccgaggc cggtcggcat cccgagcggt tctcgaaatg gctcaacatc 480

tatctgtcga gccatcttga ccggattttc ggatcgatcc tgcgcggctg a 531

<210> 25

<211> 65

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer containing Streptomyces sp CL190 DNA

<400> 25
ggggtaccgc ggccgcacgc gtctatgcac caacctttgc ggtcttgttg tcgcgttcca 60

gctgg 65

<210> 26

<211> 60

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide containing S. cerevisiae DNA

<400> 26
gagctccacc gcggcggccg cgtcgactac ggccgcagga ggagttcata tgtcagagtt 60

<210> 27

<211> 60

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide containing S. cerevisiae DNA

<400> 27
tctaccaaag gaagaggagt tttaactcga gtaggaggca catatgtctc agaacgttta 60

<210> 28

<211> 60

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide containing Streptomyces sp CL190 and
R. capsulatus DNA

<400> 28
caagaccgca aaggttggtg catagacgcg gtaaggaggc acatatgagt gagcttatac 60

<210> 29

<211> 60

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide containing R. capsulatus DNA

<400> 29
cctgcgcggc tgagcggccg cggatccgat cgcgtgcggc cgcggtaccc aattcgccct 60

<210> 30

<211> 60

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide containing Streptomyces sp CL190
and S. cerevisiae DNA

<400> 30
tgtcattgaa aagatatgag gatcctctag gtacttccct ggcgtgtgca gcggttgacg 60

<210> 31

<211> 60

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide containing Streptomyces sp CL190 DNA

<400> 31
cgattccgca ttatcggtac gggtgcctac ctagaactag tggatccccc gggctgcagg 60

<210> 32

<211> 60

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide containing N. tabacum and S. cerevisiae DNA

<400> 32
ctttcctgaa acataattta taatcagatc ggccgcagga ggagttcata tgtcagagtt 60

<210> 33

<211> 60

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide containing N. tabacum and R. capsulatus DNA

<400> 33
ttcggatcga tcctgcgcgg ctgagcggcc gatctaaaca aacccggaac agaccgttgg 60

<210> 34

<211> 59

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide containing N. tabacum and S. cerevisiae DNA

<400> 34
ctttcctgaa acataattta taatcagatc ggccgcagga ggagttcata tgtcagagt 59

<210> 35

<211> 60

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide containing N. tabacum and S. pombe DNA

<400> 35
tcgttgctaa ggatcccccg ggatccggcc gatctaaaca aacccggaac agaccgttgg 60

<210> 36

<211> 13

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide containing NotI restriction site

<400> 36
catggcggcc gcg 13

<210> 37

<211> 13

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide containing NotI restriction site

<400> 37
gatccgcggc cgc 13

<210> 38

<211> 60

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide containing S. cerevisiae DNA

<400> 38
ttaaataagg aggaataaac catggcggcc gcaggaggag ttcatatgtc agagttgaga 60

<210> 39

<211> 60

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide containing A. thaliana DNA

<400> 39
aacaacaaca acatgacccg ggatccggcc gcgatccgag ctcgagatct gcagctggta 60

<210> 40

<211> 60

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide containing S. cerevisiae DNA

<400> 40
tcgattaaat aaggaggaat aaaccatggc ggccgcagga ggagttcata tgtcagagtt 60

<210> 41

<211> 60

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide containing R. capsulatus DNA

<400> 41
gattttcgga tcgatcctgc gcggctgagc ggccgcgatc cgagctcgag atctgcagct 60

<210> 42

<211> 60

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide containing S. cerevisiae DNA

<400> 42
tcgattaaat aaggaggaat aaaccatggc ggccgcagga ggagttcata tgtcagagtt 60

<210> 43

<211> 60

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide containing S. pombe DNA

<400> 43
ttcatcgttg ctaaggatcc cccgggatcc ggccgcgatc cgagctcgag atctgcagct 60

<210> 44

<211> 61

<212> DNA

<213> Artificial Sequence

<220>
<223> Oligonucleotide containing R. capsulatus DNA

<400> 44
ttaaataagg aggaataaac catggcggcc gtaaggaggc acatatgagt gagcttatac 60

t 61

<210> 45

<211> 61

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide containing R. capsulatus DNA

<400> 45
gcctgcgcgg ctgagcggcc gcggatccga tggccgcgat ccgagctcga gatctgcagc 60

t 61

<210> 46

<211> 60

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide containing S. pombe DNA

<400> 46
ttaaataagg aggaataaac catggcggcc gtaggaggca catatgagtt cccaacaaga 60

<210> 47

<211> 60

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide containing S. pombe DNA

<400> 47
accttaattc atcgttgcta aggatccccc ggccgcgatc cgagctcgag atctgcagct 60

<210> 48

<211> 1356

<212> DNA

<213> Saccharomyces cerevisiae

<400> 48
atgtcagagt tgagagcctt cagtgcccca gggaaagcgt tactagctgg tggatattta 60

gttttagata caaaatatga agcatttgta gtcggattat cggcaagaat gcatgctgta 120

gcccatcctt acggttcatt gcaagggtct gataagtttg aagtgcgtgt gaaaagtaaa 180

caatttaaag atggggagtg gctgtaccat ataagtccta aaagtggctt cattcctgtt 240

tcgataggcg gatctaagaa ccctttcatt gaaaaagtta tcgctaacgt atttagctac 300

tttaaaccta acatggacga ctactgcaat agaaacttgt tcgttattga tattttctct 360

gatgatgcct accattctca ggaggatagc gttaccgaac atcgtggcaa cagaagattg 420

agttttcatt cgcacagaat tgaagaagtt cccaaaacag ggctgggctc ctcggcaggt 480

ttagtcacag ttttaactac agctttggcc tcctttttg tatcggacct ggaaaataat 540

gtagacaaat atagagaagt tattcataat ttagcacaag ttgctcattg tcaagctcag 600

ggtaaaattg gaagcgggtt tgatgtagcg gcggcagcat atggatctat cagatataga 660

agattcccac ccgcattaat ctctaatttg ccagatattg gaagtgctac ttacggcagt 720

aaactggcgc atttggttga tgaagaagac tggaatatta cgattaaaag taaccattta 780

ccttcgggat taactttatg gatgggcgat attaagaatg gttcagaaac agtaaaactg 840

gtccagaagg taaaaaattg gtatgattcg catatgccag aaagcttgaa aatatataca 900

gaactcgatc atgcaaattc tagatttatg gatggactat ctaaactaga tcgcttacac 960

gagactcatg acgattacag cgatcagata tttgagtctc ttgagaggaa tgactgtacc 1020

tgtcaaaagt atcctgaaat cacagaagtt agagatgcag ttgccacaat tagacgttcc 1080

tttagaaaaa taactaaaga atctggtgcc gatatcgaac ctcccgtaca aactagctta 1140

ttggatgatt gccagacctt aaaaggagtt cttacttgct taatacctgg tgctggtggt 1200

tatgacgcca ttgcagtgat tactaagcaa gatgttgatc ttagggctca aaccgctaat 1260

gacaaaagat tttctaaggt tcaatggctg gatgtaactc aggctgactg gggtgttagg 1320

aaagaaaaag atccggaaac ttatcttgat aaataa 1356

<210> 49

<211> 1332

<212> DNA

<213> Saccharomyces cerevisiae

<400> 49

atgtcattac cgttcttaac ttctgcaccg ggaaaggtta ttatttttgg tgaacactct 60

gctgtgtaca acaagcctgc cgtcgctgct agtgtgtctg cgttgagaac ctacctgcta 120

ataagcgagt catctgcacc agatactatt gaattggact tcccggacat tagctttaat 180

cataagtggt ccatcaatga tttcaatgcc atcaccgagg atcaagtaaa ctcccaaaaa 240

ttggccaagg ctcaacaagc caccgatggc ttgtctcagg aactcgttag tcttttggat 300

ccgttgttag ctcaactatc cgaatccttc cactaccatg cagcgttttg tttcctgtat 360

atgtttgttt gcctatgccc ccatgccaag aatattaagt tttctttaaa gtctacttta 420

cccatcggtg ctgggttggg ctcaagcgcc tctatttctg tatcactggc cttagctatg 480

gcctacttgg gggggttaat aggatctaat gacttggaaa agctgtcaga aaacgataag 540

catatagtga atcaatgggc cttcataggt gaaaagtgta ttcacggtac cccttcagga 600

atagataacg ctgtggccac ttatggtaat gccctgctat ttgaaaaaga ctcacataat 660

ggaacaataa acacaaacaa ttttaagttc ttagatgatt tcccagccat tccaatgatc 720

ctaacctata ctagaattcc aaggtctaca aaagatcttg ttgctcgcgt tcgtgtgttg 780

gtcaccgaga aatttcctga agttatgaag ccaattctag atgccatggg tgaatgtgcc 840

ctacaaggct tagagatcat gactaagtta agtaaatgta aaggcaccga tgacgaggct 900

gtagaaacta ataatgaact gtatgaacaa ctattggaat tgataagaat aaatcatgga 960

ctgcttgtct caatcggtgt ttctcatcct ggattagaac ttattaaaaa tctgagcgat 1020

gatttgagaa ttggctccac aaaacttacc ggtgctggtg gcggcggttg ctctttgact 1080

ttgttacgaa gagacattac tcaagagcaa attgacagct tcaaaaagaa attgcaagat 1140

gattttagtt acgagacatt tgaaacagac ttgggtggga ctggctgctg tttgttaagc 1200

gcaaaaaatt tgaataaaga tcttaaaatc aaatccctag tattccaatt atttgaaaat 1260

aaaactacca caaagcaaca aattgacgat ctattattgc caggaaacac gaatttacca 1320

tggacttcat aa 1332

<210> 50

<211> 1191

<212> DNA

<213> Saccharomyces cerevisiae

<400> 50

atgaccgttt acacagcatc cgttaccgca cccgtcaaca tcgcaaccct taagtattgg 60

gggaaaaggg acacgaagtt gaatctgccc accaattcgt ccatatcagt gactttatcg 120

caagatgacc tcagaacgtt gacctctgcg gctactgcac ctgagtttga acgcgacact 180

ttgtggttaa atggagaacc acacagcatc gacaatgaaa gaactcaaaa ttgtctgcgc 240

gacctacgcc aattaagaaa ggaaatggaa tcgaaggacg cctcattgcc cacattatct 300

caatggaaac tccacattgt ctccgaaaat aactttccta cagcagctgg tttagcttcc 360

tccgctgctg gctttgctgc attggtctct gcaattgcta agttatacca attaccacag 420

tcaacttcag aaatatctag aatagcaaga aaggggtctg gttcagcttg tagatcgttg 480

tttggcggat acgtggcctg ggaaatggga aaagctgaag atggtcatga ttccatggca 540

gtacaaatcg cagacagctc tgactggcct cagatgaaag cttgtgtcct agttgtcagc 600

gatattaaaa aggatgtgag ttccactcag ggtatgcaat tgaccgtggc aacctccgaa 660

ctatttaaag aaagaattga acatgtcgta ccaaagagat ttgaagtcat gcgtaaagcc 720

attgttgaaa aagatttcgc cacctttgca aaggaaacaa tgatggattc caactctttc 780

catgccacat gtttggactc tttccctcca atattctaca tgaatgacac ttccaagcgt 840

atcatcagtt ggtgccacac cattaatcag ttttacggag aaacaatcgt tgcatacacg 900

tttgatgcag gtccaaatgc tgtgttgtac tacttagctg aaaatgagtc gaaactcttt 960

gcatttatct ataaattgtt tggctctgtt cctggatggg acaagaaatt tactactgag 1020

cagcttgagg ctttcaacca tcaatttgaa tcatctaact ttactgcacg tgaattggat 1080

cttgagttgc aaaaggatgt tgccagagtg attttaactc aagtcggttc aggcccacaa 1140

gaaacaaacg aatctttgat tgacgcaaag actggtctac caaaggaata a 1191

<210> 51

<211> 1197

<212> DNA

<213> Saccharomyces cerevisiae

<400> 51
atgtctcaga acgtttacat tgtatcgact gccagaaccc caattggttc attccagggt 60

tctctatcct ccaagacagc agtggaattg ggtgctgttg ctttaaaagg cgccttggct 120

aaggttccag aattggatgc atccaaggat tttgacgaaa ttatttttgg taacgttctt 180

tctgccaatt tgggccaagc tccggccaga caagttgctt tggctgccgg tttgagtaat 240

catatcgttg caagcacagt taacaaggtc tgtgcatccg ctatgaaggc aatcattttg 300

ggtgctcaat ccatcaaatg tggtaatgct gatgttgtcg tagctggtgg ttgtgaatct 360

atgactaacg caccatacta catgccagca gcccgtgcgg gtgccaaatt tggccaaact 420

gttcttgttg atggtgtcga aagagatggg ttgaacgatg cgtacgatgg tctagccatg 480

ggtgtacacg cagaaaagtg tgcccgtgat tgggatatta ctagagaaca acaagacaat 540

tttgccatcg aatcctacca aaaatctcaa aaatctcaaa aggaaggtaa attcgacaat 600

gaaattgtac ctgttaccat taagggattt agaggtaagc ctgatactca agtcacgaag 660

gacgaggaac ctgctagatt acacgttgaa aaattgagat ctgcaaggac tgttttccaa 720

aaagaaaacg gtactgttac tgccgctaac gcttctccaa tcaacgatgg tgctgcagcc 780

gtcatcttgg tttccgaaaa agttttgaag gaaaagaatt tgaagccttt ggctattatc 840

aaaggttggg gtgaggccgc tcatcaacca gctgatttta catgggctcc atctcttgca 900

gttccaaagg ctttgaaaca tgctggcatc gaagacatca attctgttga ttactttgaa 960

ttcaatgaag ccttttcggt tgtcggtttg gtgaacacta agattttgaa gctagaccca 1020

tctaaggtta atgtatatgg tggtgctgtt gctctaggtc acccattggg ttgttctggt 1080

gctagagtgg ttgttacact gctatccatc ttacagcaag aaggaggtaa gatcggtgtt 1140

gccgccattt gtaatggtgg tggtggtgct tcctctattg tcattgaaaa gatatga 1197

<210> 52

<211> 1386

<212> DNA

<213> Arabidopsis thaliana

<400> 52

atggcgaaga acgttgggat tttggctatg gatatctatt tccctcccac ctgtgttcaa 60

caggaagctt tggaagcaca tgatggagca agtaaaggga aatacactat tggacttggc 120

caagattgtt tagctttttg cactgagctt gaagatgtta tctctatgag tttcaatgcg 180

gtgacatcac tttttgagaa gtataagatt gaccctaacc aaatcgggcg tcttgaagta 240

ggaagtgaga ctgttattga caaaagcaag tccatcaaga ccttcttgat gcagctcttt 300

gagaaatgtg gaaacactga tgtcgaaggt gttgactcga ccaatgcttg ctatggtgga 360

actgcagctt tgttaaactg tgtcaattgg gttgagagta actcttggga tggacgttat 420

ggcctcgtca tttgtactga cagcgcggtt tatgcagaag gacccgcaag gcccactgga 480

ggagctgcag cgattgctat gttgatagga cctgatgctc ctatcgtttt cgaaagcaaa 540

ttgagagcaa gccacatggc tcatgtctat gacttttaca agcccaatct tgctagcgag 600

tacccggttg ttgatggtaa gctttcacag acttgctacc tcatggctct tgactcctgc 660

tataaacatt tatgcaacaa gttcgagaag atcgagggca aagagttctc cataaatgat 720

gctgattaca ttgttttcca ttctccatac aataaacttg tacagaaaag ctttgctcgt 780

ctcttgtaca acgacttctt gagaaacgca agctccattg acgaggctgc caaagaaaag 840

ttcacccctt attcatcttt gacccttgac gagagttacc aaagccgtga tcttgaaaag 900

gtgtcacaac aaatttcgaa accgttttat gatgctaaag tgcaaccaac gactttaata 960

ccaaaggaag tcggtaacat gtacactgct tctctctacg ctgcatttgc ttccctcatc 1020

cacaataaac acaatgattt ggcgggaaag cgggtggtta tgttctctta tggaagtggc 1080

tccaccgcaa caatgttctc attacgcctc aacgacaata agcctccttt cagcatttca 1140

aacattgcat ctgtaatgga tgttggcggt aaattgaaag ctagacatga gtatgcacct 1200

gagaagtttg tggagacaat gaagctaatg gaacataggt atggagcaaa ggactttgtg 1260

acaaccaagg agggtattat agatcttttg gcaccgggaa cttattatct gaaagaggtt 1320

gattccttgt accggagatt ctatggcaag aaaggtgaag atggatctgt agccaatgga 1380

cactga 1386

<210> 53

<211> 1779

<212> DNA

<213> Arabidopsis thaliana

<400> 53

atggatctcc gtcggaggcc tcctaaacca ccggttacca acaacaacaa ctccaacgga 60

tctttccgtt cttatcagcc tcgcacttcc gatgacgatc atcgtcgccg ggctacaaca 120

attgctcctc caccgaaagc atccgacgcg cttcctcttc cgttatatct cacaaacgcc 180
gttttcttca cgctcttctt ctccgtcgcg tattacctcc tccaccggtg gcgtgacaag 240
atccgttaca atacgcctct tcacgtcgtc actatcacag aactcggcgc cattattgct 300
ctcatcgctt cgtttatcta tctcctaggg ttttttggta ttgactttgt tcagtcattt 360
atctcacgtg cctctggtga tgcttgggat ctcgccgata cgatcgatga tgatgaccac 420
cgccttgtca cgtgctctcc accgactccg atcgtttccg ttgctaaatt acctaatccg 480
gaacctattg ttaccgaatc gcttcctgag gaagacgagg agattgtgaa atcggttatc 540
gacggagtta ttccatcgta ctcgcttgaa tctcgtctcg gtgattgcaa aagagcggcg 600
tcgattcgtc gtgaggcgtt gcagagagtc accgggagat cgattgaagg gttaccgttg 660
gatggatttg attatgaatc gattttgggg caatgctgtg agatgcctgt tggatacatt 720
cagattcctg ttgggattgc tggtccattg ttgcttgatg gttatgagta ctctgttcct 780
atggctacaa ccgaaggttg tttggttgct agcactaaca gaggctgcaa ggctatgttt 840
atctctggtg gcgccaccag taccgttctt aaggacggta tgacccgagc acctgttgtt 900
cggttcgctt cggcgagacg agcttcggag cttaagtttt tcttggagaa tccagagaac 960
tttgatactt tggcagtagt cttcaacagg tcgagtagat ttgcaagact gcaaagtgtt 1020
aaatgcacaa tcgcggggaa gaatgcttat gtaaggttct gttgtagtac tggtgatgct 1080
atggggatga atatggtttc taaaggtgtg cagaatgttc ttgagtatct taccgatgat 1140
ttccctgaca tggatgtgat tggaatctct ggtaacttct gttcggacaa gaaacctgct 1200
gctgtgaact ggattgaggg acgtggtaaa tcagttgttt gcgaggctgt aatcagagga 1260
gagatcgtga acaaggtctt gaaaacgagc gtggctgctt tagtcgagct caacatgctc 1320
aagaacctag ctggctctgc tgttgcaggc tctctaggtg gattcaacgc tcatgccagt 1380
aacatagtgt ctgctgtatt catagctact ggccaagatc cagctcaaaa cgtggagagt 1440
tctcaatgca tcaccatgat ggaagctatt aatgacggca aagatatcca tatctcagtc 1500
actatgccat ctatcgaggt ggggacagtg ggaggaggaa cacagcttgc atctcaatca 1560
gcgtgtttaa acctgctcgg agttaaagga gcaagcacag agtcgccggg aatgaacgca 1620
aggaggctag cgacgatcgt agccggagca gttttagctg gagagttatc tttaatgtca 1680
gcaattgcag ctggacagct tgtgagaagt cacatgaaat acaatagatc cagccgagac 1740
atctctggag caacgacaac gacaacaaca acaacatga 1779

<210> 54

<211> 684

<212> DNA

<213> Artificial Sequence

<220>

<223> Schizosaccharomyces pombe IDI1 (IPP isomerase)

<400> 54
atgagttccc aacaagagaa aaaggattat gatgaagaac aattaaggtt gatggaagaa 60
gtttgtatcg ttgtagatga aaatgatgtc cctttaagat atggaacgaa aaaggagtgt 120
catttgatgg aaaatataaa taaaggtctt ttgcatagag cattctctat gttcatcttt 180
gatgagcaaa atcgcctttt acttcagcag cgtgcagaag agaaaattac atttccatcc 240
ttatggacga atacatgttg ctcccaccca ttggatgttg ctggtgaacg tggtaatact 300
ttacctgaag ctgttgaagg tgttaagaat gcagctcaac gcaagctgtt ccatgaattg 360
ggtattcaag ccaagtatat tcccaaagac aaatttcagt ttcttacacg aatccattac 420
cttgctccta gtactggtgc ttggggagag catgaaattg actacattct tttcttcaaa 480
ggtaaagttg agctggatat caatcccaat gaagttcaag cctataagta tgttactatg 540
gaagagttaa aagagatgtt ttccgatcct caatatggat tcacaccatg gttcaaactt 600
atttgtgagc attttatgtt taaatggtgg caggatgtag atcatgcgtc aaaattccaa 660
gataccttaa ttcatcgttg ctaa 684

<210> 55

<211> 531

<212> DNA

<213> Artificial Sequence

<220>

<223> Rhodobacter capsulatus idiB (IPP isomerase)

<400> 55
atgagtgagc ttatacccgc ctgggttggt gacagactgg ctccggtgga caagttggag 60
gtgcatttga aagggctccg ccacaaggcg gtgtctgttt tcgtcatgga tggcgaaaac 120
gtgctgatcc agcgccgctc ggaggagaaa tatcactctc ccgggctttg ggcgaacacc 180
tgctgcaccc atccgggctg gaccgaacgc cccgaggaat gcgcggtgcg gcggctgcgc 240
gaggagctgg ggatcaccgg gctttatccc gcccatgccg accggctgga atatcgcgcc 300
gatgtcggcg gcggcatgat cgagcatgag gtggtcgaca tctatctggc ctatgccaaa 360
ccgcatatgc ggatcacccc cgatccgcgc gaagtggccg aggtgcgctg gatcggcctt 420

tacgatctgg cggccgaggc cggtcggcat cccgagcggt tctcgaaatg gctcaacatc 480

tatctgtcga gccatcttga ccggattttc ggatcgatcc tgcgcggctg a 531

<210> 56

<211> 1059

<212> DNA

<213> Streptomyces sp.

<400> 56

atgacggaaa cgcacgccat agccggggtc ccgatgaggt gggtgggacc ccttcgtatt 60

tccgggaacg tcgccgagac cgagacccag gtcccgctcg ccacgtacga gtcgccgctg 120

tggccgtcgg tgggccgcgg ggcgaaggtc tcccggctga cggagaaggg catcgtcgcc 180

accctcgtcg acgagcggat gacccgctcg gtgatcgtcg aggcgacgga cgcgcagacc 240

gcgtacatgg ccgcgcagac catccacgcc cgcatcgacg agctgcgcga ggtggtgcgc 300

ggctgcagcc ggttcgccca gctgatcaac atcaagcacg agatcaacgc gaacctgctg 360

ttcatccggt tcgagttcac caccggtgac gcctccggcc acaacatggc cacgctcgcc 420

tccgatgtgc tcctggggca cctgctggag acgatccctg gcatctccta cggctcgatc 480

tccggcaact actgcacgga caagaaggcc accgcgatca acggcatcct cggccgcggc 540

aagaacgtga tcaccgagct gctggtgccg cgggacgtcg tcgagaacaa cctgcacacc 600

acggctgcca agatcgtcga gctgaacatc cgcaagaacc tgctcggcac cctgctcgcc 660

ggcggcatcc gctcggccaa cgcccacttc gcgaacatgc tgctcggctt ctacctggcc 720

accggccagg acgccgccaa catcgtcgag ggctcgcagg gcgtcgtcat ggccgaggac 780

cgcgacggcg acctctactt cgcctgcacc ctgccgaacc tgatcgtcgg cacggtcggc 840

aacggcaagg gtctcggctt cgtggagacg aacctcgccc ggctcggctg ccgagccgac 900

cgcgaacccg gggagaacgc ccgccgcctc gccgtcatcg cggcagcgac cgtgctgtgc 960

ggtgaactct cgctgctcgc ggcacagacg aacccgggcg aactcatgcg cgcgcacgtc 1020

cagctggaac gcgacaacaa gaccgcaaag gttggtgca 1059

<210> 57

<211> 6798

<212> DNA

<213> Artificial Sequence

<220>

<223> Streptomyces sp CL190 gene cluster containing mevalonate pathway and IPP isomerase orfs

<400> 57

tacgtacttc cctggcgtgt gcagcggttg acgcgccgtg ccctcgctgc gagcggcgcg 60

cacatctgac gtcctgcttt attgctttct cagaactcgg gacgaagcga tcccatgatc 120

acgcgatctc catgcagaaa agacaaaggg agctgagtgc gttgacacta ccgacctcgg 180

ctgaggggtt atcagaaagc caccgggccc gctcggtcgg catcggtcgc gcccacgcca 240

aggccatcct gctgggagag catgcggtcg tctacggagc gccggcactc gctctgccga 300

ttccgcagct cacggtcacg gccagcgtcg gctggtcgtc cgaggcctcc gacagtgcgg 360

gtggcctgtc ctacacgatg accggtacgc cgtcgcgggc actggtgacg caggcctccg 420

acggcctgca ccggctcacc gcggaattca tggcgcggat gggcgtgacg aacgcgccgc 480

acctcgacgt gatcctggac ggcgcgatcc cgcacggccg gggtctcggc tccagcgcgg 540

ccggctcacg cgcgatcgcc ttggccctcg ccgacctctt cggccacgaa ctggccgagc 600

acacggcgta cgaactggtg cagacggccg agaacatggc gcacggccgg gccagcggcg 660

tggacgcgat gacggtcggc gcgtcccggc cgctgctgtt ccagcagggc cgcaccgagc 720

gactggccat cggctgcgac agcctgttca tcgtcgccga cagcggcgtc ccgggcagca 780

ccaaggaagc ggtcgagatg ctgcgggagg gattcacccg cagcgccgga acacaggagc 840

ggttcgtcgg ccgggcgacg gaactgaccg aggccgcccg gcaggccctc gccgacggcc 900

ggcccgagga gctgggctcg cagctgacgt actaccacga gctgctccat gaggcccgcc 960

tgagcaccga cggcatcgat gcgctggtcg aggccgcgct gaaggcaggc agcctcggag 1020

ccaagatcac cggcggtggt ctgggcggct gcatgatcgc acaggcccgg cccgaacagg 1080

cccgggaggt cacccggcag ctccacgagg ccggtgccgt acagacctgg gtcgtaccgc 1140

tgaaagggct cgacaaccat gcgcagtgaa cacccgacca cgaccgtgct ccagtcgcgg 1200

gagcagggca gcgcggccgg cgccaccgcg gtcgcgcacc caaacatcgc gctgatcaag 1260

tactggggca agcgcgacga gcggctgatc ctgccctgca ccaccagcct gtcgatgacg 1320

ctggacgtct tccccacgac caccgaggtc cggctcgacc ccgccgccga gcacgacacg 1380

gccgccctca acggcgaggt ggccacgggc gagacgctgc gccgcatcag cgccttcctc 1440

tccctggtgc gggaggtggc gggcagcgac cagcgggccg tggtggacac ccgcaacacc 1500

gtgcccaccg gggcgggcct ggcgtcctcc gccagcgggt tcgccgccct cgccgtcgcg 1560

gccgcggccg cctacgggct cgaactcgac gaccgcgggc tgtcccggct ggcccgacgt 1620

ggatccggct ccgcctcgcg gtcgatcttc ggcggcttcg ccgtctggca cgccggcccc 1680

gacggcacgg ccacggaagc ggacctcggc tcctacgccg agccggtgcc cgcggccgac 1740

ctcgacccgg cgctggtcat cgccgtggtc aacgccggcc ccaagcccgt ctccagccgc 1800

gaggccatgc gccgcaccgt cgacacctcg ccgctgtacc ggccgtgggc cgactccagt 1860

aaggacgacc tggacgagat gcgctcggcg ctgctgcgcg gcgacctcga ggccgtgggc 1920

gagatcgcgg agcgcaacgc gctcggcatg cacgccacca tgctggccgc ccgccccgcg 1980

gtgcggtacc tgtcgccggc cacggtcacc gtgctcgaca gcgtgctcca gctccgcaag 2040

gacggtgtcc tggcctacgc gaccatggac gccggtccca acgtgaaggt gctgtgccgg 2100

cgggcggacg ccgagcgggt ggccgacgtc gtacgcgccg ccgcgtccgg cggtcaggtc 2160

ctcgtcgccg ggccgggaga cggtgcccgc ctgctgagcg agggcgcatg acgacaggtc 2220

agcgcacgat cgtccggcac gcgccgggca agctgttcgt cgcgggcgag tacgcggtcg 2280

tggatccggg caacccggcg atcctggtag cggtcgaccg gcacatcagc gtcaccgtgt 2340

ccgacgccga cgcggacacc ggggccgccg acgtcgtgat ctcctccgac ctcggtccgc 2400

aggcggtcgg ctggcgctgg cacgacggcc ggctcgtcgt ccgcgacccg gacgacgggc 2460

agcaggcgcg cagcgccctg gcccacgtgg tgtcggcgat cgagaccgtg ggccggctgc 2520

tgggcgaacg cggacagaag gtccccgctc tcaccctctc cgtcagcagc cgcctgcacg 2580

aggacggccg gaagttcggc ctgggctcca gcggcgcggt gaccgtggcg accgtagccg 2640

ccgtcgccgc gttctgcgga ctcgaactgt ccaccgacga acggttccgg ctggccatgc 2700

tcgccaccgc ggaactcgac cccaagggct ccggcgggga cctcgccgcc agcacctggg 2760

gcggctggat cgcctaccag gcgcccgacc gggcctttgt gctcgacctg gcccggcgcg 2820

tgggagtcga ccggacactg aaggcgccct ggccggggca ctcggtgcgc cgactgccgg 2880

cgcccaaggg cctcaccctg gaggtcggct ggaccggaga gcccgcctcc accgcgtccc 2940

tggtgtccga tctgcaccgc cgcacctggc ggggcagcgc ctcccaccag aggttcgtcg 3000

agaccacgac cgactgtgtc cgctccgcgg tcaccgccct ggagtccggc gacgacacga 3060

gcctgctgca cgagatccgc cgggcccgcc aggagctggc ccgcctggac gacgaggtcg 3120

gcctcggcat cttcacaccc aagctgacgg cgctgtgcga cgccgccgaa gccgtcggcg 3180

gcgcggccaa gccctccggg gcaggcggcg gcgactgcgg catcgccctg ctggacgccg 3240

aggcgtcgcg ggacatcaca catgtacggc aacggtggga gacagccggg gtgctgcccc 3300

tgcccctgac tcctgccctg gaagggatct aagaatgacc agcgcccaac gcaaggacga 3360

ccacgtacgg ctcgccatcg agcagcacaa cgcccacagc ggacgcaacc agttcgacga 3420

cgtgtcgttc gtccaccacg ccctggccgg catcgaccgg ccggacgtgt ccctggccac 3480

gtccttcgcc gggatctcct ggcaggtgcc gatctacatc aacgcgatga ccggcggcag 3540

cgagaagacc ggcctcatca accgggacct ggccaccgcc gcccgcgaga ccggcgtccc 3600

catcgcgtcc gggtccatga acgcgtacat caaggacccc tcctgcgccg acacgttccg 3660

tgtgctgcgc gacgagaacc ccaacgggtt cgtcatcgcg aacatcaacg ccaccacgac 3720
ggtcgacaac gcgcagcgcg cgatcgacct gatcgaggcg aacgccctgc agatccacat 3780
caacacggcg caggagacgc cgatgccgga gggcgaccgg tcgttcgcgt cctgggtccc 3840
gcagatcgag aagatcgcgg cggccgtcga catccccgtg atcgtcaagg aggtcggcaa 3900
cggcctgagc cggcagacca tcctgctgct cgccgacctc ggcgtgcagg cggcggacgt 3960
cagcggccgc ggcggcacgg acttcgcccg catcgagaac ggccgccggg agctcggcga 4020
ctacgcgttc ctgcacggct gggggcagtc caccgccgcc tgcctgctgg acgcccagga 4080
catctccctg cccgtcctcg cctccggcgg tgtgcgtcac ccgctcgacg tggtccgcgc 4140
cctcgcgctc ggcgcccgcg ccgtcggctc ctccgccggc ttcctgcgca ccctgatgga 4200
cgacggcgtc gacgcgctga tcacgaagct cacgacctgg ctggaccagc tggcggcgct 4260
gcagaccatg ctcggcgcgc gcaccccggc cgacctcacc cgctgcgacg tgctgctcca 4320
cggcgagctg cgtgacttct gcgccgaccg gggcatcgac acgcgccgcc tcgcccagcg 4380
ctccagctcc atcgaggccc tccagacgac gggaagcaca cgatgacgga aacgcacgcc 4440
atagccgggg tcccgatgag gtgggtggga ccccttcgta tttccgggaa cgtcgccgag 4500
accgagaccc aggtcccgct cgccacgtac gagtcgccgc tgtggccgtc ggtgggccgc 4560
ggggcgaagg tctcccggct gacggagaag ggcatcgtcg ccaccctcgt cgacgagcgg 4620
atgacccgct cggtgatcgt cgaggcgacg gacgcgcaga ccgcgtacat ggccgcgcag 4680
accatccacg cccgcatcga cgagctgcgc gaggtggtgc gcggctgcag ccggttcgcc 4740
cagctgatca acatcaagca cgagatcaac gcgaacctgc tgttcatccg gttcgagttc 4800
accaccggtg acgcctccgg ccacaacatg gccacgctcg cctccgatgt gctcctgggg 4860
cacctgctgg agacgatccc tggcatctcc tacggctcga tctccggcaa ctactgcacg 4920
gacaagaagg ccaccgcgat caacggcatc ctcggccgcg gcaagaacgt gatcaccgag 4980
ctgctggtgc cgcgggacgt cgtcgagaac aacctgcaca ccacggctgc caagatcgtc 5040
gagctgaaca tccgcaagaa cctgctcggc accctgctcg ccggcggcat ccgctcggcc 5100
aacgcccact tcgcgaacat gctgctcggc ttctacctgg ccaccggcca ggacgccgcc 5160
aacatcgtcg agggctcgca gggcgtcgtc atggccgagg accgcgacgg cgacctctac 5220
ttcgcctgca ccctgccgaa cctgatcgtc ggcacggtcg gcaacggcaa gggtctcggc 5280
ttcgtggaga cgaacctcgc ccggctcggc tgccgagccg accgcgaacc cggggagaac 5340
gcccgccgcc tcgccgtcat cgcggcagcg accgtgctgt gcggtgaact ctcgctgctc 5400
gcggcacaga cgaacccggg cgaactcatg cgcgcgcacg tccagctgga acgcgacaac 5460
aagaccgcaa aggttggtgc atagggcatg tccatctcca taggcattca cgacctgtcg 5520
ttcgccacaa ccgagttcgt cctgccgcac acggcgctcg ccgagtacaa cggcaccgag 5580

atcggcaagt accacgtcgg catcggccag cagtcgatga gcgtgccggc cgccgacgag 5640

gacatcgtga ccatggccgc gaccgcggcg cggcccatca tcgagcgcaa cggcaagagc 5700

cggatccgca cggtcgtgtt cgccacggag tcgtcgatcg accaggcgaa ggcgggcggc 5760

gtgtacgtgc actccctgct ggggctggag tcggcctgcc gggtcgtcga gctgaagcag 5820

gcctgctacg gggccaccgc cgcccttcag ttcgccatcg gcctggtgcg gcgcgacccc 5880

gcccagcagg tcctggtcat cgccagtgac gtctccaagt acgagctgga cagccccggc 5940

gaggcgaccc agggcgcggc cgcggtggcc atgctggtcg gcgccgaccc ggccctgctg 6000

cgtatcgagg agccgtcggg cctgttcacc gccgacgtca tggacttctg gcggcccaac 6060

tacctcacca ccgctctggt cgacggccag gagtccatca acgcctacct gcaggccgtc 6120

gagggcgcct ggaaggacta cgcggagcag gacggccggt cgctggagga gttcgcggcg 6180

ttcgtctacc accagccgtt cacgaagatg gcctacaagg cgcaccgcca cctgctgaac 6240

ttcaacggct acgacaccga caaggacgcc atcgagggcg ccctcggcca gacgacggcg 6300

tacaacaacg tcatcggcaa cagctacacc gcgtcggtgt acctgggcct ggccgccctg 6360

ctcgaccagg cggacgacct gacgggccgt tccatcggct tcctgagcta cggctcgggc 6420

agcgtcgccg agttcttctc gggcaccgtc gtcgccgggt accgcgagcg tctgcgcacc 6480

gaggcgaacc aggaggcgat cgcccggcgc aagagcgtcg actacgccac ctaccgcgag 6540

ctgcacgagt acacgctccc gtccgacggc ggcgaccacg ccaccccggt gcagaccacc 6600

ggcccttcc ggctggccgg gatcaacgac cacaagcgca tctacgaggc gcgctagcga 6660

cacccctcgg caacggggtg cgccactgtt cggcgcaccc cgtgccgggc tttcgcacag 6720

ctattcacga ccatttgagg ggcgggcagc cgcatgaccg acgtccgatt ccgcattatc 6780

ggtacgggtg cctacgta 6798

<210> 58

<211> 7693

<212> DNA

<213> Artificial Sequence

<220>

<223> Operon containing A. thaliana and S. cerevisiae DNA

<400> 58

ggccgcgtcg acgccggcgg aggcacatat gtctcagaac gtttacattg tatcgactgc 60

cagaacccca attggttcat tccagggttc tctatcctcc aagacagcag tggaattggg 120

tgctgttgct ttaaaaggcg ccttggctaa ggttccagaa ttggatgcat ccaaggattt 180

tgacgaaatt atttttggta acgttctttc tgccaatttg ggccaagctc cggccagaca 240
agttgctttg gctgccggtt tgagtaatca tatcgttgca agcacagtta acaaggtctg 300
tgcatccgct atgaaggcaa tcattttggg tgctcaatcc atcaaatgtg gtaatgctga 360
tgttgtcgta gctggtggtt gtgaatctat gactaacgca ccatactaca tgccagcagc 420
ccgtgcgggt gccaaatttg gccaaactgt tcttgttgat ggtgtcgaaa gagatgggtt 480
gaacgatgcg tacgatggtc tagccatggg tgtacacgca gaaaagtgtg cccgtgattg 540
ggatattact agagaacaac aagacaattt tgccatcgaa tcctaccaaa aatctcaaaa 600
atctcaaaag gaaggtaaat tcgacaatga aattgtacct gttaccatta agggatttag 660
aggtaagcct gatactcaag tcacgaagga cgaggaacct gctagattac acgttgaaaa 720
attgagatct gcaaggactg ttttccaaaa agaaaacggt actgttactg ccgctaacgc 780
ttctccaatc aacgatggtg ctgcagccgt catcttggtt tccgaaaaag ttttgaagga 840
aaagaatttg aagcctttgg ctattatcaa aggttggggt gaggccgctc atcaaccagc 900
tgattttaca tgggctccat ctcttgcagt tccaaaggct ttgaaacatg ctggcatcga 960
agacatcaat tctgttgatt actttgaatt caatgaagcc ttttcggttg tcggtttggt 1020
gaacactaag attttgaagc tagacccatc taaggttaat gtatatggtg gtgctgttgc 1080
tctaggtcac ccattgggtt gttctggtgc tagagtggtt gttacactgc tatccatctt 1140
acagcaagaa ggaggtaaga tcggtgttgc cgccatttgt aatggtggtg gtggtgcttc 1200
ctctattgtc attgaaaaga tatgaggatc ctctagatgc gcaggaggca catatggcga 1260
agaacgttgg gattttggct atggatatct atttccctcc cacctgtgtt caacaggaag 1320
ctttggaagc acatgatgga gcaagtaaag ggaaatacac tattggactt ggccaagatt 1380
gtttagcttt ttgcactgag cttgaagatg ttatctctat gagtttcaat gcggtgacat 1440
cacttttga gaagtataag attgacccta accaaatcgg gcgtcttgaa gtaggaagtg 1500
agactgttat tgacaaaagc aagtccatca agaccttctt gatgcagctc tttgagaaat 1560
gtggaaacac tgatgtcgaa ggtgttgact cgaccaatgc ttgctatggt ggaactgcag 1620
ctttgttaaa ctgtgtcaat tgggttgaga gtaactcttg ggatggacgt tatggcctcg 1680
tcatttgtac tgacagcgcg gtttatgcag aaggacccgc aaggcccact ggaggagctg 1740
cagcgattgc tatgttgata ggtcctgatg ctcctatcgt tttcgaaagc aaattgagag 1800
caagccacat ggctcatgtc tatgactttt acaagcccaa tcttgctagc gagtacccgg 1860
ttgttgatgg taagctttca cagacttgct acctcatggc tcttgactcc tgctataaac 1920
atttatgcaa caagttcgag aagatcgagg gcaaagagtt ctccataaat gatgctgatt 1980
acattgtttt ccattctcca tacaataaac ttgtacagaa aagctttgct cgtctcttgt 2040
acaacgactt cttgagaaac gcaagctcca ttgacgaggc tgccaaagaa aagttcaccc 2100

cttattcatc tttgaccctt gacgagagtt accaaagccg tgatcttgaa aaggtgtcac 2160
aacaaattgc gaaaccgttt tatgatgcta aagtgcaacc aacgacttta ataccaaagg 2220
aagtcggtaa catgtacact gcttctctct acgctgcatt tgcttccctc atccacaaga 2280
aacacaatga tttggcggga aagcgggtgg ttatgttctc ttatggaagt ggctcaaccg 2340
caacaatgtt ctcattacgc ctcaacgaca ataagcctcc tttcagcatt tcaaacattg 2400
catctgtaat ggatgttggc ggtaaattga aagctagaca tgagtatgca cctgagaagt 2460
ttgtggagac aatgaagcta atggaacata ggtatggagc aaaggacttt gtgacaacca 2520
aggagggtat tatagatctt ttggcaccgg gaacttatta tctgaaagag gttgattcct 2580
tgtaccggag attctatggc aagaaaggtg aagatggatc tgtagccaat ggacactgag 2640
gatccgtcga gcacgtggag gcacatatgc aatgctgtga gatgcctgtt ggatacattc 2700
agattcctgt tgggattgct ggtccattgt tgcttgatgg ttatgagtac tctgttccta 2760
tggctacaac cgaaggttgt ttggttgcta gcactaacag aggctgcaag gctatgttta 2820
tctctggtgg cgccaccagt accgttctta aggacggtat gacccgagca cctgttgttc 2880
ggttcgcttc ggcgagacga gcttcggagc ttaagttttt cttggagaat ccagagaact 2940
ttgatacttt ggcagtagtc ttcaacaggt cgagtagatt tgcaagactg caaagtgtta 3000
aatgcacaat cgcggggaag aatgcttatg taaggttctg ttgtagtact ggtgatgcta 3060
tggggatgaa tatggtttct aaaggtgtgc agaatgttct tgagtatctt accgatgatt 3120
tccctgacat ggatgtgatt ggaatctctg gtaacttctg ttcggacaag aaacctgctg 3180
ctgtgaactg gattgaggga cgtggtaaat cagttgtttg cgaggctgta atcagaggag 3240
agatcgtgaa caaggtcttg aaaacgagcg tggctgcttt agtcgagctc aacatgctca 3300
agaacctagc tggctctgct gttgcaggct ctctaggtgg attcaacgct catgccagta 3360
acatagtgtc tgctgtattc atagctactg gccaagatcc agctcaaaac gtggagagtt 3420
ctcaatgcat caccatgatg gaagctatta atgacggcaa agatatccat atctcagtca 3480
ctatgccatc tatcgaggtg gggacagtgg gaggaggaac acagcttgca tctcaatcag 3540
cgtgtttaaa cctgctcgga gttaaaggag caagcacaga gtcgccggga atgaacgcaa 3600
ggaggctagc gacgatcgta gccggagcag ttttagctgg agagttatct ttaatgtcag 3660
caattgcagc tggacagctt gtgagaagtc acatgaaata caatagatcc agccgagaca 3720
tctctggagc aacgacaacg acaacaacaa caacatgacc cgggatccgg ccgcaggagg 3780
agttcatatg tcagagttga gagccttcag tgccccaggg aaagcgttac tagctggtgg 3840
atatttagtt ttagatacaa aatatgaagc atttgtagtc ggattatcgg caagaatgca 3900
tgctgtagcc catccttacg gttcattgca agggtctgat aagtttgaag tgcgtgtgaa 3960
aagtaaacaa tttaaagatg gggagtggct gtaccatata agtcctaaaa gtggcttcat 4020

tcctgtttcg ataggcggat ctaagaaccc tttcattgaa aaagttatcg ctaacgtatt 4080
tagctacttt aaacctaaca tggacgacta ctgcaataga aacttgttcg ttattgatat 4140
tttctctgat gatgcctacc attctcagga ggatagcgtt accgaacatc gtggcaacag 4200
aagattgagt tttcattcgc acagaattga agaagttccc aaaacagggc tgggctcctc 4260
ggcaggttta gtcacagttt taactacagc tttggcctcc ttttttgtat cggacctgga 4320
aaataatgta gacaaatata gagaagttat tcataattta gcacaagttg ctcattgtca 4380
agctcagggt aaaattggaa gcgggtttga tgtagcggcg gcagcatatg gatctatcag 4440
atatagaaga ttcccacccg cattaatctc taatttgcca gatattggaa gtgctactta 4500
cggcagtaaa ctggcgcatt tggttgatga agaagactgg aatattacga ttaaaagtaa 4560
ccatttacct tcgggattaa ctttatggat gggcgatatt aagaatggtt cagaaacagt 4620
aaaactggtc cagaaggtaa aaaattggta tgattcgcat atgccagaaa gcttgaaaat 4680
atatacagaa ctcgatcatg caaattctag atttatggat ggactatcta aactagatcg 4740
cttacacgag actcatgacg attacagcga tcagatattt gagtctcttg agaggaatga 4800
ctgtacctgt caaaagtatc ctgaaatcac agaagttaga gatgcagttg ccacaattag 4860
acgttccttt agaaaaataa ctaaagaatc tggtgccgat atcgaacctc ccgtacaaac 4920
tagcttattg gatgattgcc agaccttaaa aggagttctt acttgcttaa tacctggtgc 4980
tggtggttat gacgccattg cagtgattac taagcaagat gttgatctta gggctcaaac 5040
cgctaatgac aaaagatttt ctaaggttca atggctggat gtaactcagg ctgactgggg 5100
tgttaggaaa gaaaaagatc cggaaactta tcttgataaa ctgcaggagg agttttaatg 5160
tcattaccgt tcttaacttc tgcaccggga aaggttatta tttttggtga acactctgct 5220
gtgtacaaca agcctgccgt cgctgctagt gtgtctgcgt tgagaaccta cctgctaata 5280
agcgagtcat ctgcaccaga tactattgaa ttggacttcc cggacattag ctttaatcat 5340
aagtggtcca tcaatgattt caatgccatc accgaggatc aagtaaactc ccaaaaattg 5400
gccaaggctc aacaagccac cgatggcttg tctcaggaac tcgttagtct tttggatccg 5460
ttgttagctc aactatccga atccttccac taccatgcag cgttttgttt cctgtatatg 5520
tttgtttgcc tatgccccca tgccaagaat attaagtttt ctttaaagtc tactttaccc 5580
atcggtgctg ggttgggctc aagcgcctct atttctgtat cactggcctt agctatggcc 5640
tacttggggg ggttaatagg atctaatgac ttggaaaagc tgtcagaaaa cgataagcat 5700
atagtgaatc aatgggcctt cataggtgaa aagtgtattc acggtacccc ttcaggaata 5760
gataacgctg tggccactta tggtaatgcc ctgctatttg aaaaagactc acataatgga 5820
acaataaaca caaacaattt taagttctta gatgatttcc cagccattcc aatgatccta 5880
acctatacta gaattccaag gtctacaaaa gatcttgttg ctcgcgttcg tgtgttggtc 5940

accgagaaat ttcctgaagt tatgaagcca attctagatg ccatgggtga atgtgcccta 6000
caaggcttag agatcatgac taagttaagt aaatgtaaag gcaccgatga cgaggctgta 6060
gaaactaata atgaactgta tgaacaacta ttggaattga taagaataaa tcatggactg 6120
cttgtctcaa tcggtgtttc tcatcctgga ttagaactta ttaaaaatct gagcgatgat 6180
ttgagaattg gctccacaaa acttaccggt gctggtggcg gcggttgctc tttgactttg 6240
ttacgaagag acattactca agagcaaatt gacagcttca aaaagaaatt gcaagatgat 6300
tttagttacg agacatttga aacagacttg ggtgggactg gctgctgttt gttaagcgca 6360
aaaaatttga ataaagatct taaaatcaaa tccctagtat tccaattatt tgaaaataaa 6420
actaccacaa agcaacaaat tgacgatcta ttattgccag gaaacacgaa tttaccatgg 6480
acttcacagg aggagtttta atgactgtat atactgctag tgtaactgct ccggtaaata 6540
ttgctactct taagtattgg gggaaaaggg acacgaagtt gaatctgccc accaattcgt 6600
ccatatcagt gactttatcg caagatgacc tcagaacgtt gacctctgcg gctactgcac 6660
ctgagtttga acgcgacact ttgtggttaa atggagaacc acacagcatc gacaatgaaa 6720
gaactcaaaa ttgtctgcgc gacctacgcc aattaagaaa ggaaatggaa tcgaaggacg 6780
cctcattgcc cacattatct caatggaaac tccacattgt ctccgaaaat aactttccta 6840
cagcagctgg tttagcttcc tccgctgctg gctttgctgc attggtctct gcaattgcta 6900
agttatacca attaccacag tcaacttcag aaatatctag aatagcaaga aaggggtctg 6960
gttcagcttg tagatcgttg tttggcggat acgtggcctg ggaaatggga aaagctgaag 7020
atggtcatga ttccatggca gtacaaatcg cagacagctc tgactggcct cagatgaaag 7080
cttgtgtcct agttgtcagc gatattaaaa aggatgtgag ttccactcag ggtatgcaat 7140
tgaccgtggc aacctccgaa ctatttaaag aaagaattga acatgtcgta ccaaagagat 7200
ttgaagtcat gcgtaaagcc attgttgaaa aagatttcgc cacctttgca aaggaaacaa 7260
tgatggattc caactctttc catgccacat gtttggactc tttccctcca atattctaca 7320
tgaatgacac ttccaagcgt atcatcagtt ggtgccacac cattaatcag ttttacggag 7380
aaacaatcgt tgcatacacg tttgatgcag gtccaaatgc tgtgttgtac tacttagctg 7440
aaaatgagtc gaaactcttt gcatttatct ataaattgtt tggctctgtt cctggatggg 7500
acaagaaatt tactactgag cagcttgagg ctttcaacca tcaatttgaa tcatctaact 7560
ttactgcacg tgaattggat cttgagttgc aaaaggatgt tgccagagtg attttaactc 7620
aagtcggttc aggcccacaa gaaacaaacg aatctttgat tgacgcaaag actggtctac 7680
caaaggaata act 7693

<210> 59

<211> 7695

<212> DNA

<213> Artificial Sequence

<220>

<223> Operon B containing A. thaliana and S. cerevisiae DNA

<400> 59

ggccgcagga ggagttcata tgtcagagtt gagagccttc agtgccccag ggaaagcgtt 60

actagctggt ggatatttag ttttagatac aaaatatgaa gcatttgtag tcggattatc 120

ggcaagaatg catgctgtag cccatcctta cggttcattg caagggtctg ataagtttga 180

agtgcgtgtg aaaagtaaac aatttaaaga tggggagtgg ctgtaccata taagtcctaa 240

aagtggcttc attcctgttt cgataggcgg atctaagaac cctttcattg aaaaagttat 300

cgctaacgta tttagctact ttaaacctaa catggacgac tactgcaata gaaacttgtt 360

cgttattgat attttctctg atgatgccta ccattctcag gaggatagcg ttaccgaaca 420

tcgtggcaac agaagattga gttttcattc gcacagaatt gaagaagttc ccaaaacagg 480

gctgggctcc tcggcaggtt tagtcacagt tttaactaca gctttggcct cctttttgt 540

atcggacctg gaaaataatg tagacaaata tagagaagtt attcataatt tagcacaagt 600

tgctcattgt caagctcagg gtaaaattgg aagcgggttt gatgtagcgg cggcagcata 660

tggatctatc agatatagaa gattcccacc cgcattaatc tctaatttgc cagatattgg 720

aagtgctact tacggcagta aactggcgca tttggttgat gaagaagact ggaatattac 780

gattaaaagt aaccatttac cttcgggatt aactttatgg atgggcgata ttaagaatgg 840

ttcagaaaca gtaaaactgg tccagaaggt aaaaaattgg tatgattcgc atatgccaga 900

aagcttgaaa atatatacag aactcgatca tgcaaattct agatttatgg atggactatc 960

taaactagat cgcttacacg agactcatga cgattacagc gatcagatat ttgagtctct 1020

tgagaggaat gactgtacct gtcaaaagta tcctgaaatc acagaagtta gagatgcagt 1080

tgccacaatt agacgttcct ttagaaaaat aactaaagaa tctggtgccg atatcgaacc 1140

tcccgtacaa actagcttat tggatgattg ccagacctta aaaggagttc ttacttgctt 1200

aatacctggt gctggtggtt atgacgccat tgcagtgatt actaagcaag atgttgatct 1260

tagggctcaa accgctaatg acaaaagatt ttctaaggtt caatggctgg atgtaactca 1320

ggctgactgg ggtgttagga aagaaaaaga tccggaaact tatcttgata aactgcagga 1380

ggagttttaa tgtcattacc gttcttaact tctgcaccgg gaaaggttat tatttttggt 1440

gaacactctg ctgtgtacaa caagcctgcc gtcgctgcta gtgtgtctgc gttgagaacc 1500

tacctgctaa taagcgagtc atctgcacca gatactattg aattggactt cccggacatt 1560

agctttaatc ataagtggtc catcaatgat ttcaatgcca tcaccgagga tcaagtaaac 1620
tcccaaaaat tggccaaggc tcaacaagcc accgatggct tgtctcagga actcgttagt 1680
cttttggatc cgttgttagc tcaactatcc gaatccttcc actaccatgc agcgttttgt 1740
ttcctgtata tgtttgtttg cctatgcccc catgccaaga atattaagtt ttctttaaag 1800
tctactttac ccatcggtgc tgggttgggc tcaagcgcct ctatttctgt atcactggcc 1860
ttagctatgg cctacttggg ggggttaata ggatctaatg acttggaaaa gctgtcagaa 1920
aacgataagc atatagtgaa tcaatgggcc ttcataggtg aaaagtgtat tcacggtacc 1980
ccttcaggaa tagataacgc tgtggccact tatggtaatg ccctgctatt tgaaaaagac 2040
tcacataatg gaacaataaa cacaaacaat tttaagttct tagatgattt cccagccatt 2100
ccaatgatcc taacctatac tagaattcca aggtctacaa aagatcttgt tgctcgcgtt 2160
cgtgtgttgg tcaccgagaa atttcctgaa gttatgaagc caattctaga tgccatgggt 2220
gaatgtgccc tacaaggctt agagatcatg actaagttaa gtaaatgtaa aggcaccgat 2280
gacgaggctg tagaaactaa taatgaactg tatgaacaac tattggaatt gataagaata 2340
aatcatggac tgcttgtctc aatcggtgtt tctcatcctg gattagaact tattaaaaat 2400
ctgagcgatg atttgagaat tggctccaca aaacttaccg gtgctggtgg cggcggttgc 2460
tctttgactt tgttacgaag agacattact caagagcaaa ttgacagctt caaaaagaaa 2520
ttgcaagatg attttagtta cgagacattt gaaacagact tgggtgggac tggctgctgt 2580
ttgttaagcg caaaaaattt gaataaagat cttaaaatca aatccctagt attccaatta 2640
tttgaaaata aaactaccac aaagcaacaa attgacgatc tattattgcc aggaaacacg 2700
aatttaccat ggacttcaga cgaggagttt taatgactgt atatactgct agtgtaactg 2760
ctccggtaaa tattgctact cttaagtatt gggggaaaag ggacacgaag ttgaatctgc 2820
ccaccaattc gtccatatca gtgactttat cgcaagatga cctcagaacg ttgacctctg 2880
cggctactgc acctgagttt gaacgcgaca ctttgtggtt aaatggagaa ccacacagca 2940
tcgacaatga aagaactcaa aattgtctgc gcgacctacg ccaattaaga aaggaaatgg 3000
aatcgaagga cgcctcattg cccacattat ctcaatggaa actccacatt gtctccgaaa 3060
ataactttcc tacagcagct ggtttagctt cctccgctgc tggctttgct gcattggtct 3120
ctgcaattgc taagttatac caattaccac agtcaacttc agaaatatct agaatagcaa 3180
gaaaggggtc tggttcagct tgtagatcgt tgtttggcgg atacgtggcc tgggaaatgg 3240
gaaaagctga agatggtcat gattccatgg cagtacaaat cgcagacagc tctgactggc 3300
ctcagatgaa agcttgtgtc ctagttgtca gcgatattaa aaaggatgtg agttccactc 3360
agggtatgca attgaccgtg gcaacctccg aactatttaa agaaagaatt gaacatgtcg 3420
taccaaagag atttgaagtc atgcgtaaag ccattgttga aaaagatttc gccacctttg 3480

caaaggaaac aatgatggat tccaactctt tccatgccac atgtttggac tctttccctc 3540
caatattcta catgaatgac acttccaagc gtatcatcag ttggtgccac accattaatc 3600
agttttacgg agaaacaatc gttgcataca cgtttgatgc aggtccaaat gctgtgttgt 3660
actacttagc tgaaaatgag tcgaaactct ttgcatttat ctataaattg tttggctctg 3720
ttcctggatg ggacaagaaa tttactactg agcagcttga ggctttcaac catcaatttg 3780
aatcatctaa ctttactgca cgtgaattgg atcttgagtt gcaaaaggat gttgccagag 3840
tgattttaac tcaagtcggt tcaggcccac aagaaacaaa cgaatctttg attgacgcaa 3900
agactggtct accaaaggaa gaggagtttt aactcgacgc cggcggaggc acatatgtct 3960
cagaacgttt acattgtatc gactgccaga accccaattg gttcattcca gggttctcta 4020
tcctccaaga cagcagtgga attgggtgct gttgctttaa aaggcgcctt ggctaaggtt 4080
ccagaattgg atgcatccaa ggattttgac gaaattattt ttggtaacgt tctttctgcc 4140
aatttgggcc aagctccggc cagacaagtt gctttggctg ccggtttgag taatcatatc 4200
gttgcaagca cagttaacaa ggtctgtgca tccgctatga aggcaatcat tttgggtgct 4260
caatccatca aatgtggtaa tgctgatgtt gtcgtagctg gtggttgtga atctatgact 4320
aacgcaccat actacatgcc agcagcccgt gcgggtgcca aatttggcca aactgttctt 4380
gttgatggtg tcgaaagaga tgggttgaac gatgcgtacg atggtctagc catgggtgta 4440
cacgcagaaa agtgtgcccg tgattgggat attactagag aacaacaaga caattttgcc 4500
atcgaatcct accaaaaatc tcaaaaatct caaaaggaag gtaaattcga caatgaaatt 4560
gtacctgtta ccattaaggg atttagaggt aagcctgata ctcaagtcac gaaggacgag 4620
gaacctgcta gattacacgt tgaaaaattg agatctgcaa ggactgtttt ccaaaaagaa 4680
aacggtactg ttactgccgc taacgcttct ccaatcaacg atggtgctgc agccgtcatc 4740
ttggtttccg aaaaagtttt gaaggaaaag aatttgaagc ctttggctat tatcaaaggt 4800
tggggtgagg ccgctcatca accagctgat tttacatggg ctccatctct tgcagttcca 4860
aaggctttga aacatgctgg catcgaagac atcaattctg ttgattactt tgaattcaat 4920
gaagcctttt cggttgtcgg tttggtgaac actaagattt tgaagctaga cccatctaag 4980
gttaatgtat atggtggtgc tgttgctcta ggtcacccat tgggttgttc tggtgctaga 5040
gtggttgtta cactgctatc catcttacag caagaaggag gtaagatcgg tgttgccgcc 5100
atttgtaatg gtggtggtgg tgcttcctct attgtcattg aaaagatatg aggatcctct 5160
agatgcgcag gaggcacata tggcgaagaa cgttgggatt ttggctatgg atatctattt 5220
ccctcccacc tgtgttcaac aggaagcttt ggaagcacat gatggagcaa gtaaagggaa 5280
atacactatt ggacttggcc aagattgttt agctttttgc actgagcttg aagatgttat 5340
ctctatgagt ttcaatgcgg tgacatcact ttttgagaag tataagattg accctaacca 5400

aatcgggcgt cttgaagtag gaagtgagac tgttattgac aaaagcaagt ccatcaagac 5460
cttcttgatg cagctctttg agaaatgtgg aaacactgat gtcgaaggtg ttgactcgac 5520
caatgcttgc tatggtggaa ctgcagcttt gttaaactgt gtcaattggg ttgagagtaa 5580
ctcttgggat ggacgttatg gcctcgtcat ttgtactgac agcgcggttt atgcagaagg 5640
acccgcaagg cccactggag gagctgcagc gattgctatg ttgataggac ctgatgctcc 5700
tatcgttttc gaaagcaaat tgagagcaag ccacatggct catgtctatg acttttacaa 5760
gcccaatctt gctagcgagt acccggttgt tgatggtaag ctttcacaga cttgctacct 5820
catggctctt gactcctgct ataaacattt atgcaacaag ttcgagaaga tcgagggcaa 5880
agagttctcc ataaatgatg ctgattacat tgttttccat tctccataca ataaacttgt 5940
acagaaaagc tttgctcgtc tcttgtacaa cgacttcttg agaaacgcaa gctccattga 6000
cgaggctgcc aaagaaaagt tcacccctta ttcatctttg acccttgacg agagttacca 6060
aagccgtgat cttgaaaagg tgtcacaaca aatttcgaaa ccgttttatg atgctaaagt 6120
gcaaccaacg actttaatac caaaggaagt cggtaacatg tacactgctt ctctctacgc 6180
tgcatttgct tccctcatcc acaataaaca caatgatttg gcgggaaagc gggtggttat 6240
gttctcttat ggaagtggct ccaccgcaac aatgttctca ttacgcctca acgacaataa 6300
gcctcctttc agcatttcaa acattgcatc tgtaatggat gttggcggta aattgaaagc 6360
tagacatgag tatgcacctg agaagtttgt ggagacaatg aagctaatgg aacataggta 6420
tggagcaaag gactttgtga caaccaagga gggtattata gatcttttgg caccgggaac 6480
ttattatctg aaagaggttg attccttgta ccggagattc tatggcaaga aaggtgaaga 6540
tggatctgta gccaatggac actgaggatc cgtcgagcac gtggaggcac atatgcaatg 6600
ctgtgagatg cctgttggat acattcagat tcctgttggg attgctggtc cattgttgct 6660
tgatggttat gagtactctg ttcctatggc tacaaccgaa ggttgtttgg ttgctagcac 6720
taacagaggc tgcaaggcta tgtttatctc tggtggcgcc accagtaccg ttcttaagga 6780
cggtatgacc cgagcacctg ttgttcggtt cgcttcggcg agacgagctt cggagcttaa 6840
gtttttcttg gagaatccag agaactttga tactttggca gtagtcttca acaggtcgag 6900
tagatttgca agactgcaaa gtgttaaatg cacaatcgcg gggaagaatg cttatgtaag 6960
gttctgttgt agtactggtg atgctatggg gatgaatatg gtttctaaag gtgtgcagaa 7020
tgttcttgag tatcttaccg atgatttccc tgacatggat gtgattggaa tctctggtaa 7080
cttctgttcg gacaagaaac ctgctgctgt gaactggatt gagggacgtg gtaaatcagt 7140
tgtttgcgag gctgtaatca gaggagagat cgtgaacaag gtcttgaaaa cgagcgtggc 7200
tgctttagtc gagctcaaca tgctcaagaa cctagctggc tctgctgttg caggctctct 7260
aggtggattc aacgctcatg ccagtaacat agtgtctgct gtattcatag ctactggcca 7320

agatccagct caaaacgtgg agagttctca atgcatcacc atgatggaag ctattaatga 7380

cggcaaagat atccatatct cagtcactat gccatctatc gaggtgggga cagtgggagg 7440

aggaacacag cttgcatctc aatcagcgtg tttaaacctg ctcggagtta aaggagcaag 7500

cacagagtcg ccgggaatga acgcaaggag gctagcgacg atcgtagccg gagcagtttt 7560

agctggagag ttatctttaa tgtcagcaat tgcagctgga cagcttgtga gaagtcacat 7620

gaaatacaat agatccagcc gagacatctc tggagcaacg acaacgacaa caacaacaac 7680

atgacccggg atccg 7695

<210> 60

<211> 8235

<212> DNA

<213> Artificial Sequence

<220>

<223> Operon C containing A. thaliana, S. cerevisiae, and R. caosulatus DNA

<400> 60

ggccgcagga ggagttcata tgtcagagtt gagagccttc agtgccccag ggaaagcgtt 60

actagctggt ggatatttag ttttagatac aaaatatgaa gcatttgtag tcggattatc 120

ggcaagaatg catgctgtag cccatcctta cggttcattg caagggtctg ataagtttga 180

agtgcgtgtg aaaagtaaac aatttaaaga tggggagtgg ctgtaccata taagtcctaa 240

aagtggcttc attcctgttt cgataggcgg atctaagaac cctttcattg aaaaagttat 300

cgctaacgta tttagctact ttaaacctaa catggacgac tactgcaata gaaacttgtt 360

cgttattgat attttctctg atgatgccta ccattctcag gaggatagcg ttaccgaaca 420

tcgtggcaac agaagattga gttttcattc gcacagaatt gaagaagttc ccaaaacagg 480

gctgggctcc tcggcaggtt tagtcacagt tttaactaca gctttggcct cctttttgt 540

atcggacctg gaaaataatg tagacaaata tagagaagtt attcataatt tagcacaagt 600

tgctcattgt caagctcagg gtaaaattgg aagcgggttt gatgtagcgg cggcagcata 660

tggatctatc agatatagaa gattcccacc cgcattaatc tctaatttgc cagatattgg 720

aagtgctact tacggcagta aactggcgca tttggttgat gaagaagact ggaatattac 780

gattaaaagt aaccatttac cttcgggatt aactttatgg atgggcgata ttaagaatgg 840

ttcagaaaca gtaaaactgg tccagaaggt aaaaaattgg tatgattcgc atatgccaga 900

aagcttgaaa atatatacag aactcgatca tgcaaattct agatttatgg atggactatc 960

taaactagat cgcttacacg agactcatga cgattacagc gatcagatat ttgagtctct 1020

tgagaggaat gactgtacct gtcaaaagta tcctgaaatc acagaagtta gagatgcagt 1080

tgccacaatt agacgttcct ttagaaaaat aactaaagaa tctggtgccg atatcgaacc 1140

tcccgtacaa actagcttat tggatgattg ccagacctta aaaggagttc ttacttgctt 1200

aatacctggt gctggtggtt atgacgccat tgcagtgatt actaagcaag atgttgatct 1260

tagggctcaa accgctaatg acaaaagatt ttctaaggtt caatggctgg atgtaactca 1320

ggctgactgg ggtgttagga aagaaaaaga tccggaaact tatcttgata aactgcagga 1380

ggagttttaa tgtcattacc gttcttaact tctgcaccgg gaaaggttat tatttttggt 1440

gaacactctg ctgtgtacaa caagcctgcc gtcgctgcta gtgtgtctgc gttgagaacc 1500

tacctgctaa taagcgagtc atctgcacca gatactattg aattggactt cccggacatt 1560

agctttaatc ataagtggtc catcaatgat ttcaatgcca tcaccgagga tcaagtaaac 1620

tcccaaaaat tggccaaggc tcaacaagcc accgatggct tgtctcagga actcgttagt 1680

cttttggatc cgttgttagc tcaactatcc gaatccttcc actaccatgc agcgttttgt 1740

ttcctgtata tgtttgtttg cctatgcccc catgccaaga atattaagtt ttctttaaag 1800

tctactttac ccatcggtgc tgggttgggc tcaagcgcct ctatttctgt atcactggcc 1860

ttagctatgg cctacttggg ggggttaata ggatctaatg acttggaaaa gctgtcagaa 1920

aacgataagc atatagtgaa tcaatgggcc ttcataggtg aaaagtgtat tcacggtacc 1980

ccttcaggaa tagataacgc tgtggccact tatggtaatg ccctgctatt tgaaaaagac 2040

tcacataatg gaacaataaa cacaaacaat tttaagttct tagatgattt cccagccatt 2100

ccaatgatcc taacctatac tagaattcca aggtctacaa aagatcttgt tgctcgcgtt 2160

cgtgtgttgg tcaccgagaa atttcctgaa gttatgaagc caattctaga tgccatgggt 2220

gaatgtgccc tacaaggctt agagatcatg actaagttaa gtaaatgtaa aggcaccgat 2280

gacgaggctg tagaaactaa taatgaactg tatgaacaac tattggaatt gataagaata 2340

aatcatggac tgcttgtctc aatcggtgtt tctcatcctg gattagaact tattaaaaat 2400

ctgagcgatg atttgagaat tggctccaca aaacttaccg gtgctggtgg cggcggttgc 2460

tctttgactt tgttacgaag agacattact caagagcaaa ttgacagctt caaaaagaaa 2520

ttgcaagatg attttagtta cgagacattt gaaacagact tgggtgggac tggctgctgt 2580

ttgttaagcg caaaaaattt gaataaagat cttaaaatca aatccctagt attccaatta 2640

tttgaaaata aaactaccac aaagcaacaa attgacgatc tattattgcc aggaaacacg 2700

aatttaccat ggacttcaga cgaggagttt taatgactgt atatactgct agtgtaactg 2760

ctccggtaaa tattgctact cttaagtatt gggggaaaag ggacacgaag ttgaatctgc 2820

ccaccaattc gtccatatca gtgactttat cgcaagatga cctcagaacg ttgacctctg 2880

cggctactgc acctgagttt gaacgcgaca ctttgtggtt aaatggagaa ccacacagca 2940

tcgacaatga aagaactcaa aattgtctgc gcgacctacg ccaattaaga aaggaaatgg 3000

aatcgaagga cgcctcattg cccacattat ctcaatggaa actccacatt gtctccgaaa 3060

ataactttcc tacagcagct ggtttagctt cctccgctgc tggctttgct gcattggtct 3120

ctgcaattgc taagttatac caattaccac agtcaacttc agaaatatct agaatagcaa 3180

gaaaggggtc tggttcagct tgtagatcgt tgtttggcgg atacgtggcc tgggaaatgg 3240

gaaaagctga agatggtcat gattccatgg cagtacaaat cgcagacagc tctgactggc 3300

ctcagatgaa agcttgtgtc ctagttgtca gcgatattaa aaaggatgtg agttccactc 3360

agggtatgca attgaccgtg gcaacctccg aactatttaa agaaagaatt gaacatgtcg 3420

taccaaagag atttgaagtc atgcgtaaag ccattgttga aaaagatttc gccacctttg 3480

caaaggaaac aatgatggat tccaactctt tccatgccac atgtttggac tctttccctc 3540

caatattcta catgaatgac acttccaagc gtatcatcag ttggtgccac accattaatc 3600

agttttacgg agaaacaatc gttgcataca cgtttgatgc aggtccaaat gctgtgttgt 3660

actacttagc tgaaaatgag tcgaaactct ttgcatttat ctataaattg tttggctctg 3720

ttcctggatg ggacaagaaa tttactactg agcagcttga ggctttcaac catcaatttg 3780

aatcatctaa ctttactgca cgtgaattgg atcttgagtt gcaaaaggat gttgccagag 3840

tgattttaac tcaagtcggt tcaggcccac aagaaacaaa cgaatctttg attgacgcaa 3900

agactggtct accaaaggaa gaggagtttt aactcgacgc cggcggaggc acatatgtct 3960

cagaacgttt acattgtatc gactgccaga accccaattg gttcattcca gggttctcta 4020

tcctccaaga cagcagtgga attgggtgct gttgctttaa aaggcgcctt ggctaaggtt 4080

ccagaattgg atgcatccaa ggattttgac gaaattattt ttggtaacgt tctttctgcc 4140

aatttgggcc aagctccggc cagacaagtt gctttggctg ccggtttgag taatcatatc 4200

gttgcaagca cagttaacaa ggtctgtgca tccgctatga aggcaatcat tttgggtgct 4260

caatccatca aatgtggtaa tgctgatgtt gtcgtagctg gtggttgtga atctatgact 4320

aacgcaccat actacatgcc agcagcccgt gcgggtgcca aatttggcca aactgttctt 4380

gttgatggtg tcgaaagaga tgggttgaac gatgcgtacg atggtctagc catgggtgta 4440

cacgcagaaa agtgtgcccg tgattgggat attactagag aacaacaaga caattttgcc 4500

atcgaatcct accaaaaatc tcaaaaatct caaaaggaag gtaaattcga caatgaaatt 4560

gtacctgtta ccattaaggg atttagaggt aagcctgata ctcaagtcac gaaggacgag 4620

gaacctgcta gattacacgt tgaaaaattg agatctgcaa ggactgtttt ccaaaaagaa 4680

aacggtactg ttactgccgc taacgcttct ccaatcaacg atggtgctgc agccgtcatc 4740

ttggtttccg aaaaagtttt gaaggaaaag aatttgaagc ctttggctat tatcaaaggt 4800

tggggtgagg ccgctcatca accagctgat tttacatggg ctccatctct tgcagttcca 4860

aaggctttga aacatgctgg catcgaagac atcaattctg ttgattactt tgaattcaat 4920
gaagcctttt cggttgtcgg tttggtgaac actaagattt tgaagctaga cccatctaag 4980
gttaatgtat atggtggtgc tgttgctcta ggtcacccat tgggttgttc tggtgctaga 5040
gtggttgtta cactgctatc catcttacag caagaaggag gtaagatcgg tgttgccgcc 5100
atttgtaatg gtggtggtgg tgcttcctct attgtcattg aaaagatatg aggatcctct 5160
agatgcgcag gaggcacata tggcgaagaa cgttgggatt ttggctatgg atatctattt 5220
ccctcccacc tgtgttcaac aggaagcttt ggaagcacat gatggagcaa gtaaagggaa 5280
atacactatt ggacttggcc aagattgttt agctttttgc actgagcttg aagatgttat 5340
ctctatgagt ttcaatgcgg tgacatcact ttttgagaag tataagattg accctaacca 5400
aatcgggcgt cttgaagtag gaagtgagac tgttattgac aaaagcaagt ccatcaagac 5460
cttcttgatg cagctctttg agaaatgtgg aaacactgat gtcgaaggtg ttgactcgac 5520
caatgcttgc tatggtggaa ctgcagcttt gttaaactgt gtcaattggg ttgagagtaa 5580
ctcttgggat ggacgttatg gcctcgtcat ttgtactgac agcgcggttt atgcagaagg 5640
acccgcaagg cccactggag gagctgcagc gattgctatg ttgataggac ctgatgctcc 5700
tatcgttttc gaaagcaaat tgagagcaag ccacatggct catgtctatg acttttacaa 5760
gcccaatctt gctagcgagt acccggttgt tgatggtaag ctttcacaga cttgctacct 5820
catggctctt gactcctgct ataaacattt atgcaacaag ttcgagaaga tcgagggcaa 5880
agagttctcc ataaatgatg ctgattacat tgttttccat tctccataca ataaacttgt 5940
acagaaaagc tttgctcgtc tcttgtacaa cgacttcttg agaaacgcaa gctccattga 6000
cgaggctgcc aaagaaaagt tcacccctta ttcatctttg acccttgacg agagttacca 6060
aagccgtgat cttgaaaagg tgtcacaaca aatttcgaaa ccgttttatg atgctaaagt 6120
gcaaccaacg actttaatac caaaggaagt cggtaacatg tacactgctt ctctctacgc 6180
tgcatttgct tccctcatcc acaataaaca caatgatttg gcgggaaagc gggtggttat 6240
gttctcttat ggaagtggct ccaccgcaac aatgttctca ttacgcctca acgacaataa 6300
gcctcctttc agcatttcaa acattgcatc tgtaatggat gttggcggta aattgaaagc 6360
tagacatgag tatgcacctg agaagtttgt ggagacaatg aagctaatgg aacataggta 6420
tggagcaaag gactttgtga caaccaagga gggtattata gatcttttgg caccgggaac 6480
ttattatctg aaagaggttg attccttgta ccggagattc tatggcaaga aaggtgaaga 6540
tggatctgta gccaatggac actgaggatc cgtcgagcac gtggaggcac atatgcaatg 6600
ctgtgagatg cctgttggat acattcagat tcctgttggg attgctggtc cattgttgct 6660
tgatggttat gagtactctg ttcctatggc tacaaccgaa ggttgtttgg ttgctagcac 6720
taacagaggc tgcaaggcta tgtttatctc tggtggcgcc accagtaccg ttcttaagga 6780

cggtatgacc cgagcacctg ttgttcggtt cgcttcggcg agacgagctt cggagcttaa 6840

gtttttcttg gagaatccag agaactttga tactttggca gtagtcttca acaggtcgag 6900

tagatttgca agactgcaaa gtgttaaatg cacaatcgcg gggaagaatg cttatgtaag 6960

gttctgttgt agtactggtg atgctatggg gatgaatatg gtttctaaag gtgtgcagaa 7020

tgttcttgag tatcttaccg atgatttccc tgacatggat gtgattggaa tctctggtaa 7080

cttctgttcg gacaagaaac ctgctgctgt gaactggatt gagggacgtg gtaaatcagt 7140

tgtttgcgag gctgtaatca gaggagagat cgtgaacaag gtcttgaaaa cgagcgtggc 7200

tgctttagtc gagctcaaca tgctcaagaa cctagctggc tctgctgttg caggctctct 7260

aggtggattc aacgctcatg ccagtaacat agtgtctgct gtattcatag ctactggcca 7320

agatccagct caaaacgtgg agagttctca atgcatcacc atgatggaag ctattaatga 7380

cggcaaagat atccatatct cagtcactat gccatctatc gaggtgggga cagtgggagg 7440

aggaacacag cttgcatctc aatcagcgtg tttaaacctg ctcggagtta aaggagcaag 7500

cacagagtcg ccgggaatga acgcaaggag gctagcgacg atcgtagccg gagcagtttt 7560

agctggagag ttatctttaa tgtcagcaat tgcagctgga cagcttgtga gaagtcacat 7620

gaaatacaat agatccagcc gagacatctc tggagcaacg acaacgacaa caacaacaac 7680

atgacccgta aggaggcaca tatgagtgag cttatacccg cctgggttgg tgacagactg 7740

gctccggtgg acaagttgga ggtgcatttg aaagggctcc gccacaaggc ggtgtctgtt 7800

ttcgtcatgg atggcgaaaa cgtgctgatc cagcgccgct cggaggagaa atatcactct 7860

cccgggcttt gggcgaacac ctgctgcacc catccgggct ggaccgaacg ccccgaggaa 7920

tgcgcggtgc ggcggctgcg cgaggagctg gggatcaccg ggctttatcc cgcccatgcc 7980

gaccggctgg aatatcgcgc cgatgtcggc ggcggcatga tcgagcatga ggtggtcgac 8040

atctatctgg cctatgccaa accgcatatg cggatcaccc ccgatccgcg cgaagtggcc 8100

gaggtgcgct ggatcggcct ttacgatctg gcggccgagg ccggtcggca tcccgagcgg 8160

ttctcgaaat ggctcaacat ctatctgtcg agccatcttg accggatttt cggatcgatc 8220

ctgcgcggct gagcg 8235

<210> 61

<211> 7681

<212> DNA

<213> Artificial Sequence

<220>

<223> Operon C containing A. thaliana, S. cerevisiae, and Streptomyces sp CL190

DNA, and R. capsulatus DNA

<400> 61
ggccgcgtcg actacggccg caggaggagt tcatatgtca gagttgagag ccttcagtgc 60
cccagggaaa gcgttactag ctggtggata tttagtttta gatacaaaat atgaagcatt 120
tgtagtcgga ttatcggcaa gaatgcatgc tgtagcccat ccttacggtt cattgcaagg 180
gtctgataag tttgaagtgc gtgtgaaaag taaacaattt aaagatgggg agtggctgta 240
ccatataagt cctaaaagtg gcttcattcc tgtttcgata ggcggatcta agaacccttt 300
cattgaaaaa gttatcgcta acgtatttag ctactttaaa cctaacatgg acgactactg 360
caatagaaac ttgttcgtta ttgatatttt ctctgatgat gcctaccatt ctcaggagga 420
tagcgttacc gaacatcgtg gcaacagaag attgagtttt cattcgcaca gaattgaaga 480
agttcccaaa acagggctgg gctcctcggc aggtttagtc acagttttaa ctacagcttt 540
ggcctccttt tttgtatcgg acctggaaaa taatgtagac aaatatagag aagttattca 600
taatttagca caagttgctc attgtcaagc tcagggtaaa attggaagcg ggtttgatgt 660
agcggcggca gcatatggat ctatcagata tagaagattc ccacccgcat taatctctaa 720
tttgccagat attggaagtg ctacttacgg cagtaaactg gcgcatttgg ttgatgaaga 780
agactggaat attacgatta aaagtaacca tttaccttcg ggattaactt tatggatggg 840
cgatattaag aatggttcag aaacagtaaa actggtccag aaggtaaaaa attggtatga 900
ttcgcatatg ccagaaagct tgaaaatata tacagaactc gatcatgcaa attctagatt 960
tatggatgga ctatctaaac tagatcgctt acacgagact catgacgatt acagcgatca 1020
gatatttgag tctcttgaga ggaatgactg tacctgtcaa aagtatcctg aaatcacaga 1080
agttagagat gcagttgcca caattagacg ttcctttaga aaaataacta aagaatctgg 1140
tgccgatatc gaacctcccg tacaaactag cttattggat gattgccaga ccttaaaagg 1200
agttcttact tgcttaatac ctggtgctgg tggttatgac gccattgcag tgattactaa 1260
gcaagatgtt gatcttaggg ctcaaaccgc taatgacaaa agattttcta aggttcaatg 1320
gctggatgta actcaggctg actggggtgt taggaaagaa aaagatccgg aaacttatct 1380
tgataaactg caggaggagt tttaatgtca ttaccgttct taacttctgc accgggaaag 1440
gttattattt ttggtgaaca ctctgctgtg tacaacaagc ctgccgtcgc tgctagtgtg 1500
tctgcgttga gaacctacct gctaataagc gagtcatctg caccagatac tattgaattg 1560
gacttcccgg acattagctt taatcataag tggtccatca atgatttcaa tgccatcacc 1620
gaggatcaag taaactccca aaaattggcc aaggctcaac aagccaccga tggcttgtct 1680
caggaactcg ttagtctttt ggatccgttg ttagctcaac tatccgaatc cttccactac 1740
catgcagcgt tttgtttcct gtatatgttt gtttgcctat gcccccatgc caagaatatt 1800

aagttttctt taaagtctac tttacccatc ggtgctgggt tgggctcaag cgcctctatt 1860

tctgtatcac tggccttagc tatggcctac ttgggggggt taataggatc taatgacttg 1920

gaaaagctgt cagaaaacga taagcatata gtgaatcaat gggccttcat aggtgaaaag 1980

tgtattcacg gtacccccttc aggaatagat aacgctgtgg ccacttatgg taatgccctg 2040

ctatttgaaa aagactcaca taatggaaca ataaacacaa acaattttaa gttcttagat 2100

gatttcccag ccattccaat gatcctaacc tatactagaa ttccaaggtc tacaaaagat 2160

cttgttgctc gcgttcgtgt gttggtcacc gagaaatttc ctgaagttat gaagccaatt 2220

ctagatgcca tgggtgaatg tgccctacaa ggcttagaga tcatgactaa gttaagtaaa 2280

tgtaaaggca ccgatgacga ggctgtagaa actaataatg aactgtatga acaactattg 2340

gaattgataa gaataaatca tggactgctt gtctcaatcg gtgtttctca tcctggatta 2400

gaacttatta aaaatctgag cgatgatttg agaattggct ccacaaaact taccggtgct 2460

ggtggcggcg gttgctcttt gactttgtta cgaagagaca ttactcaaga gcaaattgac 2520

agcttcaaaa agaaattgca agatgatttt agttacgaga catttgaaac agacttgggt 2580

gggactggct gctgtttgtt aagcgcaaaa aatttgaata aagatcttaa aatcaaatcc 2640

ctagtattcc aattatttga aaataaaact accacaaagc aacaaattga cgatctatta 2700

ttgccaggaa acacgaattt accatggact tcagacgagg agttttaatg actgtatata 2760

ctgctagtgt aactgctccg gtaaatattg ctactcttaa gtattggggg aaaagggaca 2820

cgaagttgaa tctgcccacc aattcgtcca tatcagtgac tttatcgcaa gatgacctca 2880

gaacgttgac ctctgcggct actgcacctg agtttgaacg cgacactttg tggttaaatg 2940

gagaaccaca cagcatcgac aatgaaagaa ctcaaaattg tctgcgcgac ctacgccaat 3000

taagaaagga aatggaatcg aaggacgcct cattgcccac attatctcaa tggaaactcc 3060

acattgtctc cgaaaataac tttcctacag cagctggttt agcttcctcc gctgctggct 3120

ttgctgcatt ggtctctgca attgctaagt tataccaatt accacagtca acttcagaaa 3180

tatctagaat agcaagaaag gggtctggtt cagcttgtag atcgttgttt ggcggatacg 3240

tggcctggga aatgggaaaa gctgaagatg gtcatgattc catggcagta caaatcgcag 3300

acagctctga ctggcctcag atgaaagctt gtgtcctagt tgtcagcgat attaaaaagg 3360

atgtgagttc cactcagggt atgcaattga ccgtggcaac ctccgaacta tttaaagaaa 3420

gaattgaaca tgtcgtacca aagagatttg aagtcatgcg taaagccatt gttgaaaaag 3480

atttcgccac ctttgcaaag gaaacaatga tggattccaa ctctttccat gccacatgtt 3540

tggactcttt ccctccaata ttctacatga atgacacttc caagcgtatc atcagttggt 3600

gccacaccat taatcagttt tacggagaaa caatcgttgc atacacgttt gatgcaggtc 3660

caaatgctgt gttgtactac ttagctgaaa atgagtcgaa actctttgca tttatctata 3720

aattgtttgg ctctgttcct ggatgggaca agaaatttac tactgagcag cttgaggctt 3780
tcaaccatca atttgaatca tctaacttta ctgcacgtga attggatctt gagttgcaaa 3840
aggatgttgc cagagtgatt ttaactcaag tcggttcagg cccacaagaa acaaacgaat 3900
ctttgattga cgcaaagact ggtctaccaa aggaagagga gttttaactc gagtaggagg 3960
cacatatgtc tcagaacgtt tacattgtat cgactgccag aaccccaatt ggttcattcc 4020
agggttctct atcctccaag acagcagtgg aattgggtgc tgttgcttta aaaggcgcct 4080
tggctaaggt tccagaattg gatgcatcca aggattttga cgaaattatt tttggtaacg 4140
ttctttctgc caatttgggc caagctccgg ccagacaagt tgctttggct gccggtttga 4200
gtaatcatat cgttgcaagc acagttaaca aggtctgtgc atccgctatg aaggcaatca 4260
ttttgggtgc tcaatccatc aaatgtggta atgctgatgt tgtcgtagct ggtggttgtg 4320
aatctatgac taacgcacca tactacatgc cagcagcccg tgcgggtgcc aaatttggcc 4380
aaactgttct tgttgatggt gtcgaaagag atgggttgaa cgatgcgtac gatggtctag 4440
ccatgggtgt acacgcagaa aagtgtgccc gtgattggga tattactaga gaacaacaag 4500
acaattttgc catcgaatcc taccaaaaat ctcaaaaatc tcaaaaggaa ggtaaattcg 4560
acaatgaaat tgtacctgtt accattaagg gatttagagg taagcctgat actcaagtca 4620
cgaaggacga ggaacctgct agattacacg ttgaaaaatt gagatctgca aggactgttt 4680
tccaaaaaga aaacggtact gttactgccg ctaacgcttc tccaatcaac gatggtgctg 4740
cagccgtcat cttggtttcc gaaaaagttt tgaaggaaaa gaatttgaag cctttggcta 4800
ttatcaaagg ttggggtgag gccgctcatc aaccagctga ttttacatgg gctccatctc 4860
ttgcagttcc aaaggctttg aaacatgctg gcatcgaaga catcaattct gttgattact 4920
ttgaattcaa tgaagccttt tcggttgtcg gtttggtgaa cactaagatt ttgaagctag 4980
acccatctaa ggttaatgta tatggtggtg ctgttgctct aggtcaccca ttgggttgtt 5040
ctggtgctag agtggttgtt acactgctat ccatcttaca gcaagaagga ggtaagatcg 5100
gtgttgccgc catttgtaat ggtggtggtg gtgcttcctc tattgtcatt gaaaagatat 5160
gaggatcctc tagatgcgca ggaggcacat atggcgaaga acgttgggat tttggctatg 5220
gatatctatt tccctcccac ctgtgttcaa caggaagctt tggaagcaca tgatggagca 5280
agtaaaggga aatacactat tggacttggc caagattgtt tagcttttg cactgagctt 5340
gaagatgtta tctctatgag tttcaatgcg gtgacatcac tttttgagaa gtataagatt 5400
gaccctaacc aaatcgggcg tcttgaagta ggaagtgaga ctgttattga caaaagcaag 5460
tccatcaaga ccttcttgat gcagctcttt gagaaatgtg gaaacactga tgtcgaaggt 5520
gttgactcga ccaatgcttg ctatggtgga actgcagctt tgttaaactg tgtcaattgg 5580
gttgagagta actcttggga tggacgttat ggcctcgtca tttgtactga cagcgcggtt 5640

tatgcagaag gacccgcaag gcccactgga ggagctgcag cgattgctat gttgatagga 5700
cctgatgctc ctatcgtttt cgaaagcaaa ttgagagcaa gccacatggc tcatgtctat 5760
gacttttaca agcccaatct tgctagcgag tacccggttg ttgatggtaa gctttcacag 5820
acttgctacc tcatggctct tgactcctgc tataaacatt tatgcaacaa gttcgagaag 5880
atcgagggca aagagttctc cataaatgat gctgattaca ttgttttcca ttctccatac 5940
aataaacttg tacagaaaag ctttgctcgt ctcttgtaca acgacttctt gagaaacgca 6000
agctccattg acgaggctgc caaagaaaag ttcacccctt attcatcttt gacccttgac 6060
gagagttacc aaagccgtga tcttgaaaag gtgtcacaac aaatttcgaa accgttttat 6120
gatgctaaag tgcaaccaac gactttaata ccaaaggaag tcggtaacat gtacactgct 6180
tcctctacg ctgcatttgc ttccctcatc cacaataaac acaatgattt ggcgggaaag 6240
cgggtggtta tgttctctta tggaagtggc tccaccgcaa caatgttctc attacgcctc 6300
aacgacaata agcctccttt cagcatttca aacattgcat ctgtaatgga tgttggcggt 6360
aaattgaaag ctagacatga gtatgcacct gagaagtttg tggagacaat gaagctaatg 6420
gaacataggt atggagcaaa ggactttgtg acaaccaagg agggtattat agatcttttg 6480
gcaccgggaa cttattatct gaaagaggtt gattccttgt accggagatt ctatggcaag 6540
aaaggtgaag atggatctgt agccaatgga cactgaggat ccgtcgactc gagcacgtga 6600
ggaggcacat atgacggaaa cgcacgccat agccggggtc ccgatgaggt gggtgggacc 6660
ccttcgtatt tccgggaacg tcgccgagac cgagacccag gtcccgctcg ccacgtacga 6720
gtcgccgctg tggccgtcgg tgggccgcgg ggcgaaggtc tcccggctga cggagaaggg 6780
catcgtcgcc accctcgtcg acgagcggat gacccgctcg gtgatcgtcg aggcgacgga 6840
cgcgcagacc gcgtacatgg ccgcgcagac catccacgcc cgcatcgacg agctgcgcga 6900
ggtggtgcgc ggctgcagcc ggttcgccca gctgatcaac atcaagcacg agatcaacgc 6960
gaacctgctg ttcatccggt tcgagttcac caccggtgac gcctccggcc acaacatggc 7020
cacgctcgcc tccgatgtgc tcctggggca cctgctggag acgatccctg gcatctccta 7080
cggctcgatc tccggcaact actgcacgga caagaaggcc accgcgatca acggcatcct 7140
cggccgcggc aagaacgtga tcaccgagct gctggtgccg cgggacgtcg tcgagaacaa 7200
cctgcacacc acggctgcca agatcgtcga gctgaacatc cgcaagaacc tgctcggcac 7260
cctgctcgcc ggcggcatcc gctcggccaa cgcccacttc gcgaacatgc tgctcggctt 7320
ctacctggcc accggccagg acgccgccaa catcgtcgag ggctcgcagg gcgtcgtcat 7380
ggccgaggac cgcgacggcg acctctactt cgcctgcacc ctgccgaacc tgatcgtcgg 7440
cacggtcggc aacggcaagg gtctcggctt cgtggagacg aacctcgccc ggctcggctg 7500
ccgagccgac cgcgaacccg gggagaacgc ccgccgcctc gccgtcatcg cggcagcgac 7560

cgtgctgtgc ggtgaactct cgctgctcgc ggcacagacg aacccgggcg aactcatgcg 7620

cgcgcacgtc cagctggaac gcgacaacaa gaccgcaaag gttggtgcat agacgcgtgc 7680

g 7681

<210> 62

<211> 8224

<212> DNA

<213> Artificial Sequence

<220>

<223> Operon E containing A. thaliana, S. cerevesiae, Steptomyces sp CL190 DNA,
and R. capsulatus

<400> 62

ggccgcgtcg actacggccg caggaggagt tcatatgtca gagttgagag ccttcagtgc 60

cccagggaaa gcgttactag ctggtggata tttagtttta gatacaaaat atgaagcatt 120

tgtagtcgga ttatcggcaa gaatgcatgc tgtagcccat ccttacggtt cattgcaagg 180

gtctgataag tttgaagtgc gtgtgaaaag taaacaattt aaagatgggg agtggctgta 240

ccatataagt cctaaaagtg gcttcattcc tgtttcgata ggcggatcta agaacccttt 300

cattgaaaaa gttatcgcta acgtatttag ctactttaaa cctaacatgg acgactactg 360

caatagaaac ttgttcgtta ttgatatttt ctctgatgat gcctaccatt ctcaggagga 420

tagcgttacc gaacatcgtg gcaacagaag attgagtttt cattcgcaca gaattgaaga 480

agttcccaaa acagggctgg gctcctcggc aggtttagtc acagttttaa ctacagcttt 540

ggcctccttt tttgtatcgg acctggaaaa taatgtagac aaatatagag aagttattca 600

taatttagca caagttgctc attgtcaagc tcagggtaaa attggaagcg ggtttgatgt 660

agcggcggca gcatatggat ctatcagata tagaagattc ccacccgcat taatctctaa 720

tttgccagat attggaagtg ctacttacgg cagtaaactg gcgcatttgg ttgatgaaga 780

agactggaat attacgatta aaagtaacca tttaccttcg ggattaactt tatggatggg 840

cgatattaag aatggttcag aaacagtaaa actggtccag aaggtaaaaa attggtatga 900

ttcgcatatg ccagaaagct tgaaaatata tacagaactc gatcatgcaa attctagatt 960

tatggatgga ctatctaaac tagatcgctt acacgagact catgacgatt acagcgatca 1020

gatatttgag tctcttgaga ggaatgactg tacctgtcaa aagtatcctg aaatcacaga 1080

agttagagat gcagttgcca caattagacg ttcctttaga aaaataacta aagaatctgg 1140

tgccgatatc gaacctcccg tacaaactag cttattggat gattgccaga ccttaaaagg 1200

agttcttact tgcttaatac ctggtgctgg tggttatgac gccattgcag tgattactaa 1260
gcaagatgtt gatcttaggg ctcaaaccgc taatgacaaa agattttcta aggttcaatg 1320
gctggatgta actcaggctg actggggtgt taggaaagaa aaagatccgg aaacttatct 1380
tgataaactg caggaggagt tttaatgtca ttaccgttct taacttctgc accgggaaag 1440
gttattattt ttggtgaaca ctctgctgtg tacaacaagc ctgccgtcgc tgctagtgtg 1500
tctgcgttga gaacctacct gctaataagc gagtcatctg caccagatac tattgaattg 1560
gacttcccgg acattagctt taatcataag tggtccatca atgatttcaa tgccatcacc 1620
gaggatcaag taaactccca aaaattggcc aaggctcaac aagccaccga tggcttgtct 1680
caggaactcg ttagtctttt ggatccgttg ttagctcaac tatccgaatc cttccactac 1740
catgcagcgt tttgtttcct gtatatgttt gtttgcctat gcccccatgc caagaatatt 1800
aagttttctt taaagtctac tttacccatc ggtgctgggt tgggctcaag cgcctctatt 1860
tctgtatcac tggccttagc tatggcctac ttgggggggt taataggatc taatgacttg 1920
gaaaagctgt cagaaaacga taagcatata gtgaatcaat gggccttcat aggtgaaaag 1980
tgtattcacg gtacccctc aggaatagat aacgctgtgg ccacttatgg taatgccctg 2040
ctatttgaaa aagactcaca taatggaaca ataaacacaa acaattttaa gttcttagat 2100
gatttcccag ccattccaat gatcctaacc tatactagaa ttccaaggtc tacaaaagat 2160
cttgttgctc gcgttcgtgt gttggtcacc gagaaatttc ctgaagttat gaagccaatt 2220
ctagatgcca tgggtgaatg tgccctacaa ggcttagaga tcatgactaa gttaagtaaa 2280
tgtaaaggca ccgatgacga ggctgtagaa actaataatg aactgtatga acaactattg 2340
gaattgataa gaataaatca tggactgctt gtctcaatcg gtgtttctca tcctggatta 2400
gaacttatta aaaatctgag cgatgatttg agaattggct ccacaaaact taccggtgct 2460
ggtggcggcg gttgctcttt gactttgtta cgaagagaca ttactcaaga gcaaattgac 2520
agcttcaaaa agaaattgca agatgatttt agttacgaga catttgaaac agacttgggt 2580
gggactggct gctgtttgtt aagcgcaaaa aatttgaata aagatcttaa aatcaaatcc 2640
ctagtattcc aattatttga aaataaaact accacaaagc aacaaattga cgatctatta 2700
ttgccaggaa acacgaattt accatggact tcagacgagg agttttaatg actgtatata 2760
ctgctagtgt aactgctccg gtaaatattg ctactcttaa gtattggggg aaaagggaca 2820
cgaagttgaa tctgcccacc aattcgtcca tatcagtgac tttatcgcaa gatgacctca 2880
gaacgttgac ctctgcggct actgcacctg agtttgaacg cgacactttg tggttaaatg 2940
gagaaccaca cagcatcgac aatgaaagaa ctcaaaattg tctgcgcgac ctacgccaat 3000
taagaaagga aatggaatcg aaggacgcct cattgcccac attatctcaa tggaaactcc 3060
acattgtctc cgaaaataac tttcctacag cagctggttt agcttcctcc gctgctggct 3120

ttgctgcatt ggtctctgca attgctaagt tataccaatt accacagtca acttcagaaa 3180
tatctagaat agcaagaaag gggtctggtt cagcttgtag atcgttgttt ggcggatacg 3240
tggcctggga aatgggaaaa gctgaagatg gtcatgattc catggcagta caaatcgcag 3300
acagctctga ctggcctcag atgaaagctt gtgtcctagt tgtcagcgat attaaaaagg 3360
atgtgagttc cactcagggt atgcaattga ccgtggcaac ctccgaacta tttaaagaaa 3420
gaattgaaca tgtcgtacca aagagatttg aagtcatgcg taaagccatt gttgaaaaag 3480
atttcgccac ctttgcaaag gaaacaatga tggattccaa ctctttccat gccacatgtt 3540
tggactcttt ccctccaata ttctacatga atgacacttc caagcgtatc atcagttggt 3600
gccacaccat taatcagttt tacggagaaa caatcgttgc atacacgttt gatgcaggtc 3660
caaatgctgt gttgtactac ttagctgaaa atgagtcgaa actctttgca tttatctata 3720
aattgtttgg ctctgttcct ggatgggaca agaaatttac tactgagcag cttgaggctt 3780
tcaaccatca atttgaatca tctaacttta ctgcacgtga attggatctt gagttgcaaa 3840
aggatgttgc cagagtgatt ttaactcaag tcggttcagg cccacaagaa acaaacgaat 3900
ctttgattga cgcaaagact ggtctaccaa aggaagagga gttttaactc gagtaggagg 3960
cacatatgtc tcagaacgtt tacattgtat cgactgccag aaccccaatt ggttcattcc 4020
agggttctct atcctccaag acagcagtgg aattgggtgc tgttgcttta aaaggcgcct 4080
tggctaaggt tccagaattg gatgcatcca aggattttga cgaaattatt tttggtaacg 4140
ttctttctgc caatttgggc caagctccgg ccagacaagt tgctttggct gccggtttga 4200
gtaatcatat cgttgcaagc acagttaaca aggtctgtgc atccgctatg aaggcaatca 4260
ttttgggtgc tcaatccatc aaatgtggta atgctgatgt tgtcgtagct ggtggttgtg 4320
aatctatgac taacgcacca tactacatgc cagcagcccg tgcgggtgcc aaatttggcc 4380
aaactgttct tgttgatggt gtcgaaagag atgggttgaa cgatgcgtac gatggtctag 4440
ccatgggtgt acacgcagaa aagtgtgccc gtgattggga tattactaga gaacaacaag 4500
acaattttgc catcgaatcc taccaaaaat ctcaaaaatc tcaaaaggaa ggtaaattcg 4560
acaatgaaat tgtacctgtt accattaagg gatttagagg taagcctgat actcaagtca 4620
cgaaggacga ggaacctgct agattacacg ttgaaaaatt gagatctgca aggactgttt 4680
tccaaaaaga aaacggtact gttactgccg ctaacgcttc tccaatcaac gatggtgctg 4740
cagccgtcat cttggtttcc gaaaaagttt tgaaggaaaa gaatttgaag cctttggcta 4800
ttatcaaagg ttggggtgag gccgctcatc aaccagctga ttttacatgg gctccatctc 4860
ttgcagttcc aaaggctttg aaacatgctg gcatcgaaga catcaattct gttgattact 4920
ttgaattcaa tgaagccttt tcggttgtcg gtttggtgaa cactaagatt ttgaagctag 4980
acccatctaa ggttaatgta tatggtggtg ctgttgctct aggtcaccca ttgggttgtt 5040

ctggtgctag agtggttgtt acactgctat ccatcttaca gcaagaagga ggtaagatcg 5100

gtgttgccgc catttgtaat ggtggtggtg gtgcttcctc tattgtcatt gaaaagatat 5160

gaggatcctc tagatgcgca ggaggcacat atggcgaaga acgttgggat tttggctatg 5220

gatatctatt tccctcccac ctgtgttcaa caggaagctt tggaagcaca tgatggagca 5280

agtaaaggga aatacactat tggacttggc caagattgtt tagctttttg cactgagctt 5340

gaagatgtta tctctatgag tttcaatgcg gtgacatcac tttttgagaa gtataagatt 5400

gaccctaacc aaatcgggcg tcttgaagta ggaagtgaga ctgttattga caaaagcaag 5460

tccatcaaga ccttcttgat gcagctcttt gagaaatgtg gaaacactga tgtcgaaggt 5520

gttgactcga ccaatgcttg ctatggtgga actgcagctt tgttaaactg tgtcaattgg 5580

gttgagagta actcttggga tggacgttat ggcctcgtca tttgtactga cagcgcggtt 5640

tatgcagaag gacccgcaag gcccactgga ggagctgcag cgattgctat gttgatagga 5700

cctgatgctc ctatcgtttt cgaaagcaaa ttgagagcaa gccacatggc tcatgtctat 5760

gacttttaca agcccaatct tgctagcgag tacccggttg ttgatggtaa gctttcacag 5820

acttgctacc tcatggctct tgactcctgc tataaacatt tatgcaacaa gttcgagaag 5880

atcgagggca aagagttctc cataaatgat gctgattaca ttgttttcca ttctccatac 5940

aataaacttg tacagaaaag ctttgctcgt ctcttgtaca acgacttctt gagaaacgca 6000

agctccattg acgaggctgc caaagaaaag ttcacccctt attcatcttt gacccttgac 6060

gagagttacc aaagccgtga tcttgaaaag gtgtcacaac aaatttcgaa accgttttat 6120

gatgctaaag tgcaaccaac gactttaata ccaaaggaag tcggtaacat gtacactgct 6180

tctctctacg ctgcatttgc ttccctcatc cacaataaac acaatgattt ggcgggaaag 6240

cgggtggtta tgttctctta tggaagtggc tccaccgcaa caatgttctc attacgcctc 6300

aacgacaata agcctccttt cagcatttca aacattgcat ctgtaatgga tgttggcggt 6360

aaattgaaag ctagacatga gtatgcacct gagaagtttg tggagacaat gaagctaatg 6420

gaacataggt atggagcaaa ggactttgtg acaaccaagg agggtattat agatcttttg 6480

gcaccgggaa cttattatct gaaagaggtt gattccttgt accggagatt ctatggcaag 6540

aaaggtgaag atggatctgt agccaatgga cactgaggat ccgtcgactc gagcacgtga 6600

ggaggcacat atgacggaaa cgcacgccat agccggggtc ccgatgaggt gggtgggacc 6660

ccttcgtatt tccgggaacg tcgccgagac cgagacccag gtcccgctcg ccacgtacga 6720

gtcgccgctg tggccgtcgg tgggccgcgg ggcgaaggtc tcccggctga cggagaaggg 6780

catcgtcgcc accctcgtcg acgagcggat gacccgctcg gtgatcgtcg aggcgacgga 6840

cgcgcagacc gcgtacatgg ccgcgcagac catccacgcc cgcatcgacg agctgcgcga 6900

ggtggtgcgc ggctgcagcc ggttcgccca gctgatcaac atcaagcacg agatcaacgc 6960

gaacctgctg ttcatccggt tcgagttcac caccggtgac gcctccggcc acaacatggc 7020

cacgctcgcc tccgatgtgc tcctggggca cctgctggag acgatccctg gcatctccta 7080

cggctcgatc tccggcaact actgcacgga caagaaggcc accgcgatca acggcatcct 7140

cggccgcggc aagaacgtga tcaccgagct gctggtgccg cgggacgtcg tcgagaacaa 7200

cctgcacacc acggctgcca agatcgtcga gctgaacatc cgcaagaacc tgctcggcac 7260

cctgctcgcc ggcggcatcc gctcggccaa cgcccacttc gcgaacatgc tgctcggctt 7320

ctacctggcc accggccagg acgccgccaa catcgtcgag ggctcgcagg gcgtcgtcat 7380

ggccgaggac cgcgacggcg acctctactt cgcctgcacc ctgccgaacc tgatcgtcgg 7440

cacggtcggc aacggcaagg gtctcggctt cgtggagacg aacctcgccc ggctcggctg 7500

ccgagccgac cgcgaacccg gggagaacgc ccgccgcctc gccgtcatcg cggcagcgac 7560

cgtgctgtgc ggtgaactct cgctgctcgc ggcacagacg aacccgggcg aactcatgcg 7620

cgcgcacgtc cagctggaac gcgacaacaa gaccgcaaag gttggtgcat agacgcggta 7680

aggaggcaca tatgagtgag cttatacccg cctgggttgg tgacagactg gctccggtgg 7740

acaagttgga ggtgcatttg aaagggctcc gccacaaggc ggtgtctgtt ttcgtcatgg 7800

atggcgaaaa cgtgctgatc cagcgccgct cggaggagaa atatcactct cccgggcttt 7860

gggcgaacac ctgctgcacc catccgggct ggaccgaacg ccccgaggaa tgcgcggtgc 7920

ggcggctgcg cgaggagctg gggatcaccg ggctttatcc cgcccatgcc gaccggctgg 7980

aatatcgcgc cgatgtcggc ggcggcatga tcgagcatga ggtggtcgac atctatctgg 8040

cctatgccaa accgcatatg cggatcaccc ccgatccgcg cgaagtggcc gaggtgcgct 8100

ggatcggcct ttacgatctg gcggccgagg ccggtcggca tcccgagcgg ttctcgaaat 8160

ggctcaacat ctatctgtcg agccatcttg accggatttt cggatcgatc ctgcgcggct 8220

gagc 8224

<210> 63

<211> 8077

<212> DNA

<213> Artificial Sequence

<220>

<223> Operon F containing A. thaliana, S. cerevisiae, and Streptomyces sp CL190
DNA

<400> 63
ccaccgcggc ggccgcgtcg acgccggcgg aggcacatat gtctcagaac gtttacattg 60

tatcgactgc cagaacccca attggttcat tccagggttc tctatcctcc aagacagcag 120

tggaattggg tgctgttgct ttaaaaggcg ccttggctaa ggttccagaa ttggatgcat 180
ccaaggattt tgacgaaatt atttttggta acgttctttc tgccaatttg ggccaagctc 240
cggccagaca agttgctttg gctgccggtt tgagtaatca tatcgttgca agcacagtta 300
acaaggtctg tgcatccgct atgaaggcaa tcattttggg tgctcaatcc atcaaatgtg 360
gtaatgctga tgttgtcgta gctggtggtt gtgaatctat gactaacgca ccatactaca 420
tgccagcagc ccgtgcgggt gccaaatttg gccaaactgt tcttgttgat ggtgtcgaaa 480
gagatgggtt gaacgatgcg tacgatggtc tagccatggg tgtacacgca gaaaagtgtg 540
cccgtgattg ggatattact agagaacaac aagacaattt tgccatcgaa tcctaccaaa 600
aatctcaaaa atctcaaaag gaaggtaaat tcgacaatga aattgtacct gttaccatta 660
agggatttag aggtaagcct gatactcaag tcacgaagga cgaggaacct gctagattac 720
acgttgaaaa attgagatct gcaaggactg ttttccaaaa agaaaacggt actgttactg 780
ccgctaacgc ttctccaatc aacgatggtg ctgcagccgt catcttggtt tccgaaaaag 840
ttttgaagga aaagaatttg aagcctttgg ctattatcaa aggttggggt gaggccgctc 900
atcaaccagc tgattttaca tgggctccat ctcttgcagt tccaaaggct ttgaaacatg 960
ctggcatcga agacatcaat tctgttgatt actttgaatt caatgaagcc ttttcggttg 1020
tcggtttggt gaacactaag attttgaagc tagacccatc taaggttaat gtatatggtg 1080
gtgctgttgc tctaggtcac ccattgggtt gttctggtgc tagagtggtt gttacactgc 1140
tatccatctt acagcaagaa ggaggtaaga tcggtgttgc cgccatttgt aatggtggtg 1200
gtggtgcttc ctctattgtc attgaaaaga tatgaggatc ctctaggtac ttccctggcg 1260
tgtgcagcgg ttgacgcgcc gtgccctcgc tgcgagcggc gcgcacatct gacgtcctgc 1320
tttattgctt tctcagaact cgggacgaag cgatcccatg atcacgcgat ctccatgcag 1380
aaaagacaaa gggagctgag tgcgttgaca ctaccgacct cggctgaggg ggtatcagaa 1440
agccaccggg cccgctcggt cggcatcggt cgcgcccacg ccaaggccat cctgctggga 1500
gagcatgcgg tcgtctacgg agcgccggca ctcgctctgc cgattccgca gctcacggtc 1560
acggccagcg tcggctggtc gtccgaggcc tccgacagtg cgggtggcct gtcctacacg 1620
atgaccggta cgccgtcgcg ggcactggtg acgcaggcct ccgacggcct gcaccggctc 1680
accgcggaat tcatggcgcg gatgggcgtg acgaacgcgc cgcacctcga cgtgatcctg 1740
gacggcgcga tcccgcacgg ccggggtctc ggctccagcg cggccggctc acgcgcgatc 1800
gccttggccc tcgccgacct cttcggccac gaactggccg agcacacggc gtacgaactg 1860
gtgcagacgg ccgagaacat ggcgcacggc cgggccagcg gcgtggacgc gatgacggtc 1920
ggcgcgtccc ggccgctgct gttccagcag ggccgcaccg agcgactggc catcggctgc 1980
gacagcctgt tcatcgtcgc cgacagcggc gtcccgggca gcaccaagga agcggtcgag 2040

atgctgcggg agggattcac ccgcagcgcc ggaacacagg agcggttcgt cggccgggcg 2100
acggaactga ccgaggccgc ccggcaggcc ctcgccgacg gccggcccga ggagctgggc 2160
tcgcagctga cgtactacca cgagctgctc catgaggccc gcctgagcac cgacggcatc 2220
gatgcgctgg tcgaggccgc gctgaaggca ggcagcctcg gagccaagat caccggcggt 2280
ggtctgggcg gctgcatgat cgcacaggcc cggcccgaac aggcccggga ggtcacccgg 2340
cagctccacg aggccggtgc cgtacagacc tgggtcgtac cgctgaaagg gctcgacaac 2400
catgcgcagt gaacacccga ccacgaccgt gctccagtcg cgggagcagg gcagcgcggc 2460
cggcgccacc gcggtcgcgc acccaaacat cgcgctgatc aagtactggg gcaagcgcga 2520
cgagcggctg atcctgccct gcaccaccag cctgtcgatg acgctggacg tcttccccac 2580
gaccaccgag gtccggctcg accccgccgc cgagcacgac acggccgccc tcaacggcga 2640
ggtggccacg ggcgagacgc tgcgccgcat cagcgccttc ctctccctgg tgcgggaggt 2700
ggcgggcagc gaccagcggg ccgtggtgga cacccgcaac accgtgccca ccggggcggg 2760
cctggcgtcc tccgccagcg ggttcgccgc cctcgccgtc gcggccgcgg ccgcctacgg 2820
gctcgaactc gacgaccgcg ggctgtcccg gctggcccga cgtggatccg gctccgcctc 2880
gcggtcgatc ttcggcggct tcgccgtctg gcacgccggc cccgacggca cggccacgga 2940
agcggacctc ggctcctacg ccgagccggt gcccgcggcc gacctcgacc cggcgctggt 3000
catcgccgtg gtcaacgccg gccccaagcc cgtctccagc cgcgaggcca tgcgccgcac 3060
cgtcgacacc tcgccgctgt accggccgtg ggccgactcc agtaaggacg acctggacga 3120
gatgcgctcg gcgctgctgc gcggcgacct cgaggccgtg ggcgagatcg cggagcgcaa 3180
cgcgctcggc atgcacgcca ccatgctggc cgcccgcccc gcggtgcggt acctgtcgcc 3240
ggccacggtc accgtgctcg acagcgtgct ccagctccgc aaggacggtg tcctggccta 3300
cgcgaccatg gacgccggtc ccaacgtgaa ggtgctgtgc cggcgggcgg acgccgagcg 3360
ggtggccgac gtcgtacgcg ccgccgcgtc cggcggtcag gtcctcgtcg ccgggccggg 3420
agacggtgcc cgcctgctga gcgagggcgc atgacgacag gtcagcgcac gatcgtccgg 3480
cacgcgccgg gcaagctgtt cgtcgcgggc gagtacgcgg tcgtggatcc gggcaacccg 3540
gcgatcctgg tagcggtcga ccggcacatc agcgtcaccg tgtccgacgc cgacgcggac 3600
accggggccg ccgacgtcgt gatctcctcc gacctcggtc cgcaggcggt cggctggcgc 3660
tggcacgacg gccggctcgt cgtccgcgac ccggacgacg ggcagcaggc gcgcagcgcc 3720
ctggcccacg tggtgtcggc gatcgagacc gtgggccggc tgctgggcga acgcggacag 3780
aaggtccccg ctctcaccct ctccgtcagc agccgcctgc acgaggacgg ccggaagttc 3840
ggcctgggct ccagcggcgc ggtgaccgtg gcgaccgtag ccgccgtcgc cgcgttctgc 3900
ggactcgaac tgtccaccga cgaacggttc cggctggcca tgctcgccac cgcggaactc 3960

gaccccaagg gctccggcgg ggacctcgcc gccagcacct ggggcggctg gatcgcctac 4020
caggcgcccg accgggcctt tgtgctcgac ctggcccggc gcgtgggagt cgaccggaca 4080
ctgaaggcgc cctggccggg gcactcggtg cgccgactgc cggcgcccaa gggcctcacc 4140
ctggaggtcg gctggaccgg agagcccgcc tccaccgcgt ccctggtgtc cgatctgcac 4200
cgccgcacct ggcggggcag cgcctcccac cagaggttcg tcgagaccac gaccgactgt 4260
gtccgctccg cggtcaccgc cctggagtcc ggcgacgaca cgagcctgct gcacgagatc 4320
cgccgggccc gccaggagct ggcccgcctg gacgacgagg tcggcctcgg catcttcaca 4380
cccaagctga cggcgctgtg cgacgccgcc gaagccgtcg gcggcgcggc caagccctcc 4440
ggggcaggcg gcggcgactg cggcatcgcc ctgctggacg ccgaggcgtc gcgggacatc 4500
acacatgtac ggcaacggtg ggagacagcc ggggtgctgc ccctgcccct gactcctgcc 4560
ctggaaggga tctaagaatg accagcgccc aacgcaagga cgaccacgta cggctcgcca 4620
tcgagcagca caacgcccac agcggacgca accagttcga cgacgtgtcg ttcgtccacc 4680
acgccctggc cggcatcgac cggccggacg tgtccctggc cacgtccttc gccgggatct 4740
cctggcaggt gccgatctac atcaacgcga tgaccggcgg cagcgagaag accggcctca 4800
tcaaccggga cctggccacc gccgcccgcg agaccggcgt ccccatcgcg tccgggtcca 4860
tgaacgcgta catcaaggac ccctcctgcg ccgacacgtt ccgtgtgctg cgcgacgaga 4920
accccaacgg gttcgtcatc gcgaacatca acgccaccac gacggtcgac aacgcgcagc 4980
gcgcgatcga cctgatcgag gcgaacgccc tgcagatcca catcaacacg gcgcaggaga 5040
cgccgatgcc ggagggcgac cggtcgttcg cgtcctgggt cccgcagatc gagaagatcg 5100
cggcggccgt cgacatcccc gtgatcgtca aggaggtcgg caacggcctg agccggcaga 5160
ccatcctgct gctcgccgac ctcggcgtgc aggcggcgga cgtcagcggc cgcggcggca 5220
cggacttcgc ccgcatcgag aacggccgcc gggagctcgg cgactacgcg ttcctgcacg 5280
gctgggggca gtccaccgcc gcctgcctgc tggacgccca ggacatctcc ctgcccgtcc 5340
tcgcctccgg cggtgtgcgt cacccgctcg acgtggtccg cgccctcgcg ctcggcgccc 5400
gcgccgtcgg ctcctccgcc ggcttcctgc gcaccctgat ggacgacggc gtcgacgcgc 5460
tgatcacgaa gctcacgacc tggctggacc agctggcggc gctgcagacc atgctcggcg 5520
cgcgcacccc ggccgacctc acccgctgcg acgtgctgct ccacggcgag ctgcgtgact 5580
tctgcgccga ccggggcatc gacacgcgcc gcctcgccca gcgctccagc tccatcgagg 5640
ccctccagac gacgggaagc acacgatgac ggaaacgcac gccatagccg gggtcccgat 5700
gaggtgggtg ggaccccttc gtatttccgg gaacgtcgcc gagaccgaga cccaggtccc 5760
gctcgccacg tacgagtcgc cgctgtggcc gtcggtgggc cgcggggcga aggtctcccg 5820
gctgacggag aagggcatcg tcgccaccct cgtcgacgag cggatgaccc gctcggtgat 5880

cgtcgaggcg acggacgcgc agaccgcgta catggccgcg cagaccatcc acgcccgcat 5940
cgacgagctg cgcgaggtgg tgcgcggctg cagccggttc gcccagctga tcaacatcaa 6000
gcacgagatc aacgcgaacc tgctgttcat ccggttcgag ttcaccaccg gtgacgcctc 6060
cggccacaac atggccacgc tcgcctccga tgtgctcctg gggcacctgc tggagacgat 6120
ccctggcatc tcctacggct cgatctccgg caactactgc acggacaaga aggccaccgc 6180
gatcaacggc atcctcggcc gcggcaagaa cgtgatcacc gagctgctgg tgccgcggga 6240
cgtcgtcgag aacaacctgc acaccacggc tgccaagatc gtcgagctga acatccgcaa 6300
gaacctgctc ggcaccctgc tcgccggcgg catccgctcg gccaacgccc acttcgcgaa 6360
catgctgctc ggcttctacc tggccaccgg ccaggacgcc gccaacatcg tcgagggctc 6420
gcagggcgtc gtcatggccg aggaccgcga cggcgacctc tacttcgcct gcaccctgcc 6480
gaacctgatc gtcggcacgg tcggcaacgg caagggtctc ggcttcgtgg agacgaacct 6540
cgcccggctc ggctgccgag ccgaccgcga acccggggag aacgcccgcc gcctcgccgt 6600
catcgcggca gcgaccgtgc tgtgcggtga actctcgctg ctcgcggcac agacgaaccc 6660
gggcgaactc atgcgcgcgc acgtccagct ggaacgcgac aacaagaccg caaaggttgg 6720
tgcatagggc atgtccatct ccataggcat tcacgacctg tcgttcgcca caaccgagtt 6780
cgtcctgccg cacacggcgc tcgccgagta caacggcacc gagatcggca agtaccacgt 6840
cggcatcggc cagcagtcga tgagcgtgcc ggccgccgac gaggacatcg tgaccatggc 6900
cgcgaccgcg gcgcggccca tcatcgagcg caacggcaag agccggatcc gcacggtcgt 6960
gttcgccacg gagtcgtcga tcgaccaggc gaaggcgggc ggcgtgtacg tgcactccct 7020
gctggggctg gagtcggcct gccgggtcgt cgagctgaag caggcctgct acggggccac 7080
cgccgccctt cagttcgcca tcggcctggt gcggcgcgac cccgcccagc aggtcctggt 7140
catcgccagt gacgtctcca agtacgagct ggacagcccc ggcgaggcga cccagggcgc 7200
ggccgcggtg gccatgctgg tcggcgccga cccggccctg ctgcgtatcg aggagccgtc 7260
gggcctgttc accgccgacg tcatggactt ctggcggccc aactacctca ccaccgctct 7320
ggtcgacggc caggagtcca tcaacgccta cctgcaggcc gtcgagggcg cctggaagga 7380
ctacgcggag caggacggcc ggtcgctgga ggagttcgcg gcgttcgtct accaccagcc 7440
gttcacgaag atggcctaca aggcgcaccg ccacctgctg aacttcaacg gctacgacac 7500
cgacaaggac gccatcgagg gcgccctcgg ccagacgacg gcgtacaaca acgtcatcgg 7560
caacagctac accgcgtcgg tgtacctggg cctggccgcc ctgctcgacc aggcggacga 7620
cctgacgggc cgttccatcg gcttcctgag ctacggctcg ggcagcgtcg ccgagttctt 7680
ctcgggcacc gtcgtcgccg ggtaccgcga gcgtctgcgc accgaggcga accaggaggc 7740
gatcgcccgg cgcaagagcg tcgactacgc cacctaccgc gagctgcacg agtacacgct 7800

cccgtccgac ggcggcgacc acgccacccc ggtgcagacc accggcccct tccggctggc 7860

cgggatcaac gaccacaagc gcatctacga ggcgcgctag cgacacccct cggcaacggg 7920

gtgcgccact gttcggcgca ccccgtgccg ggctttcgca cagctattca cgaccatttg 7980

aggggcgggc agccgcatga ccgacgtccg attccgcatt atcggtacgg gtgcctacct 8040

agaactagtg gatcccccgg gctgcaggaa ttcgata 8077

<210> 64

<211> 8400

<212> DNA

<213> Artificial Sequence

<220>

<223> Operon G containing A. thaliana, S. cerevisiae, and S. pombe DNA

<400> 64

ggccgcagga ggagttcata tgtcagagtt gagagccttc agtgccccag ggaaagcgtt 60

actagctggt ggatatttag ttttagatac aaaatatgaa gcatttgtag tcggattatc 120

ggcaagaatg catgctgtag cccatcctta cggttcattg caagggtctg ataagtttga 180

agtgcgtgtg aaaagtaaac aatttaaaga tggggagtgg ctgtaccata taagtcctaa 240

aagtggcttc attcctgttt cgataggcgg atctaagaac cctttcattg aaaaagttat 300

cgctaacgta tttagctact ttaaacctaa catggacgac tactgcaata gaaacttgtt 360

cgttattgat attttctctg atgatgccta ccattctcag gaggatagcg ttaccgaaca 420

tcgtggcaac agaagattga gttttcattc gcacagaatt gaagaagttc ccaaaacagg 480

gctgggctcc tcggcaggtt tagtcacagt tttaactaca gctttggcct ccttttttgt 540

atcggacctg gaaaataatg tagacaaata tagagaagtt attcataatt tagcacaagt 600

tgctcattgt caagctcagg gtaaaattgg aagcgggttt gatgtagcgg cggcagcata 660

tggatctatc agatatagaa gattcccacc cgcattaatc tctaatttgc cagatattgg 720

aagtgctact tacggcagta aactggcgca tttggttgat gaagaagact ggaatattac 780

gattaaaagt aaccatttac cttcgggatt aactttatgg atgggcgata ttaagaatgg 840

ttcagaaaca gtaaaactgg tccagaaggt aaaaaattgg tatgattcgc atatgccaga 900

aagcttgaaa atatatacag aactcgatca tgcaaattct agatttatgg atggactatc 960

taaactagat cgcttacacg agactcatga cgattacagc gatcagatat ttgagtctct 1020

tgagaggaat gactgtacct gtcaaaagta tcctgaaatc acagaagtta gagatgcagt 1080

tgccacaatt agacgttcct ttagaaaaat aactaaagaa tctggtgccg atatcgaacc 1140

tcccgtacaa actagcttat tggatgattg ccagacctta aaaggagttc ttacttgctt 1200

aatacctggt gctggtggtt atgacgccat tgcagtgatt actaagcaag atgttgatct 1260

tagggctcaa accgctaatg acaaaagatt ttctaaggtt caatggctgg atgtaactca 1320

ggctgactgg ggtgttagga aagaaaaaga tccggaaact tatcttgata aactgcagga 1380

ggagttttaa tgtcattacc gttcttaact tctgcaccgg gaaaggttat tatttttggt 1440

gaacactctg ctgtgtacaa caagcctgcc gtcgctgcta gtgtgtctgc gttgagaacc 1500

tacctgctaa taagcgagtc atctgcacca gatactattg aattggactt cccggacatt 1560

agctttaatc ataagtggtc catcaatgat ttcaatgcca tcaccgagga tcaagtaaac 1620

tcccaaaaat tggccaaggc tcaacaagcc accgatggct tgtctcagga actcgttagt 1680

cttttggatc cgttgttagc tcaactatcc gaatccttcc actaccatgc agcgttttgt 1740

ttcctgtata tgtttgtttg cctatgcccc catgccaaga atattaagtt ttctttaaag 1800

tctactttac ccatcggtgc tgggttgggc tcaagcgcct ctatttctgt atcactggcc 1860

ttagctatgg cctacttggg ggggttaata ggatctaatg acttggaaaa gctgtcagaa 1920

aacgataagc atatagtgaa tcaatgggcc ttcataggtg aaaagtgtat tcacggtacc 1980

ccttcaggaa tagataacgc tgtggccact tatggtaatg ccctgctatt tgaaaaagac 2040

tcacataatg gaacaataaa cacaaacaat tttaagttct tagatgattt cccagccatt 2100

ccaatgatcc taacctatac tagaattcca aggtctacaa aagatcttgt tgctcgcgtt 2160

cgtgtgttgg tcaccgagaa atttcctgaa gttatgaagc caattctaga tgccatgggt 2220

gaatgtgccc tacaaggctt agagatcatg actaagttaa gtaaatgtaa aggcaccgat 2280

gacgaggctg tagaaactaa taatgaactg tatgaacaac tattggaatt gataagaata 2340

aatcatggac tgcttgtctc aatcggtgtt tctcatcctg gattagaact tattaaaaat 2400

ctgagcgatg atttgagaat tggctccaca aaacttaccg gtgctggtgg cggcggttgc 2460

tctttgactt tgttacgaag agacattact caagagcaaa ttgacagctt caaaaagaaa 2520

ttgcaagatg attttagtta cgagacattt gaaacagact tgggtgggac tggctgctgt 2580

ttgttaagcg caaaaaattt gaataaagat cttaaaatca aatccctagt attccaatta 2640

tttgaaaata aaactaccac aaagcaacaa attgacgatc tattattgcc aggaaacacg 2700

aatttaccat ggacttcaga cgaggagttt taatgactgt atatactgct agtgtaactg 2760

ctccggtaaa tattgctact cttaagtatt gggggaaaag ggacacgaag ttgaatctgc 2820

ccaccaattc gtccatatca gtgactttat cgcaagatga cctcagaacg ttgacctctg 2880

cggctactgc acctgagttt gaacgcgaca ctttgtggtt aaatggagaa ccacacagca 2940

tcgacaatga aagaactcaa aattgtctgc gcgacctacg ccaattaaga aaggaaatgg 3000

aatcgaagga cgcctcattg cccacattat ctcaatggaa actccacatt gtctccgaaa 3060

ataactttcc tacagcagct ggtttagctt cctccgctgc tggctttgct gcattggtct 3120

ctgcaattgc taagttatac caattaccac agtcaacttc agaaatatct agaatagcaa 3180

gaaaggggtc tggttcagct tgtagatcgt tgtttggcgg atacgtggcc tgggaaatgg 3240

gaaaagctga agatggtcat gattccatgg cagtacaaat cgcagacagc tctgactggc 3300

ctcagatgaa agcttgtgtc ctagttgtca gcgatattaa aaaggatgtg agttccactc 3360

agggtatgca attgaccgtg gcaacctccg aactatttaa agaaagaatt gaacatgtcg 3420

taccaaagag atttgaagtc atgcgtaaag ccattgttga aaaagatttc gccacctttg 3480

caaaggaaac aatgatggat tccaactctt tccatgccac atgtttggac tctttccctc 3540

caatattcta catgaatgac acttccaagc gtatcatcag ttggtgccac accattaatc 3600

agttttacgg agaaacaatc gttgcataca cgtttgatgc aggtccaaat gctgtgttgt 3660

actacttagc tgaaaatgag tcgaaactct ttgcatttat ctataaattg tttggctctg 3720

ttcctggatg ggacaagaaa tttactactg agcagcttga ggctttcaac catcaatttg 3780

aatcatctaa ctttactgca cgtgaattgg atcttgagtt gcaaaaggat gttgccagag 3840

tgattttaac tcaagtcggt tcaggcccac aagaaacaaa cgaatctttg attgacgcaa 3900

agactggtct accaaaggaa gaggagtttt aactcgacgc cggcggaggc acatatgtct 3960

cagaacgttt acattgtatc gactgccaga accccaattg gttcattcca gggttctcta 4020

tcctccaaga cagcagtgga attgggtgct gttgctttaa aaggcgcctt ggctaaggtt 4080

ccagaattgg atgcatccaa ggattttgac gaaattattt ttggtaacgt tctttctgcc 4140

aatttgggcc aagctccggc cagacaagtt gctttggctg ccggtttgag taatcatatc 4200

gttgcaagca cagttaacaa ggtctgtgca tccgctatga aggcaatcat tttgggtgct 4260

caatccatca aatgtggtaa tgctgatgtt gtcgtagctg gtggttgtga atctatgact 4320

aacgcaccat actacatgcc agcagcccgt gcgggtgcca aatttggcca aactgttctt 4380

gttgatggtg tcgaaagaga tgggttgaac gatgcgtacg atggtctagc catgggtgta 4440

cacgcagaaa agtgtgcccg tgattgggat attactagag aacaacaaga caattttgcc 4500

atcgaatcct accaaaaatc tcaaaaatct caaaaggaag gtaaattcga caatgaaatt 4560

gtacctgtta ccattaaggg atttagaggt aagcctgata ctcaagtcac gaaggacgag 4620

gaacctgcta gattacacgt tgaaaaattg agatctgcaa ggactgtttt ccaaaaagaa 4680

aacggtactg ttactgccgc taacgcttct ccaatcaacg atggtgctgc agccgtcatc 4740

ttggtttccg aaaaagtttt gaaggaaaag aatttgaagc ctttggctat tatcaaaggt 4800

tggggtgagg ccgctcatca accagctgat tttacatggg ctccatctct tgcagttcca 4860

aaggctttga aacatgctgg catcgaagac atcaattctg ttgattactt tgaattcaat 4920

gaagcctttt cggttgtcgg tttggtgaac actaagattt tgaagctaga cccatctaag 4980

gttaatgtat atggtggtgc tgttgctcta ggtcacccat tgggttgttc tggtgctaga 5040

gtggttgtta cactgctatc catcttacag caagaaggag gtaagatcgg tgttgccgcc 5100
atttgtaatg gtggtggtgg tgcttcctct attgtcattg aaaagatatg aggatcctct 5160
agatgcgcag gaggcacata tggcgaagaa cgttgggatt ttggctatgg atatctattt 5220
ccctcccacc tgtgttcaac aggaagcttt ggaagcacat gatggagcaa gtaaagggaa 5280
atacactatt ggacttggcc aagattgttt agctttttgc actgagcttg aagatgttat 5340
ctctatgagt ttcaatgcgg tgacatcact ttttgagaag tataagattg accctaacca 5400
aatcgggcgt cttgaagtag gaagtgagac tgttattgac aaaagcaagt ccatcaagac 5460
cttcttgatg cagctctttg agaaatgtgg aaacactgat gtcgaaggtg ttgactcgac 5520
caatgcttgc tatggtggaa ctgcagcttt gttaaactgt gtcaattggg ttgagagtaa 5580
ctcttgggat ggacgttatg gcctcgtcat ttgtactgac agcgcggttt atgcagaagg 5640
acccgcaagg cccactggag gagctgcagc gattgctatg ttgataggac ctgatgctcc 5700
tatcgttttc gaaagcaaat tgagagcaag ccacatggct catgtctatg acttttacaa 5760
gcccaatctt gctagcgagt acccggttgt tgatggtaag ctttcacaga cttgctacct 5820
catggctctt gactcctgct ataaacattt atgcaacaag ttcgagaaga tcgagggcaa 5880
agagttctcc ataaatgatg ctgattacat tgttttccat tctccataca ataaacttgt 5940
acagaaaagc tttgctcgtc tcttgtacaa cgacttcttg agaaacgcaa gctccattga 6000
cgaggctgcc aaagaaaagt tcacccctta ttcatctttg acccttgacg agagttacca 6060
aagccgtgat cttgaaaagg tgtcacaaca aatttcgaaa ccgttttatg atgctaaagt 6120
gcaaccaacg actttaatac caaaggaagt cggtaacatg tacactgctt ctctctacgc 6180
tgcatttgct tccctcatcc acaataaaca caatgatttg gcgggaaagc gggtggttat 6240
gttctcttat ggaagtggct ccaccgcaac aatgttctca ttacgcctca acgacaataa 6300
gcctcctttc agcatttcaa acattgcatc tgtaatggat gttggcggta aattgaaagc 6360
tagacatgag tatgcacctg agaagtttgt ggagacaatg aagctaatgg aacataggta 6420
tggagcaaag gactttgtga caaccaagga gggtattata gatcttttgg caccgggaac 6480
ttattatctg aaagaggttg attccttgta ccggagattc tatggcaaga aaggtgaaga 6540
tggatctgta gccaatggac actgaggatc cgtcgagcac gtggaggcac atatgcaatg 6600
ctgtgagatg cctgttggat acattcagat tcctgttggg attgctggtc cattgttgct 6660
tgatggttat gagtactctg ttcctatggc tacaaccgaa ggttgtttgg ttgctagcac 6720
taacagaggc tgcaaggcta tgtttatctc tggtggcgcc accagtaccg ttcttaagga 6780
cggtatgacc cgagcacctg ttgttcggtt cgcttcggcg agacgagctt cggagcttaa 6840
gtttttcttg gagaatccag agaactttga tactttggca gtagtcttca acaggtcgag 6900
tagatttgca agactgcaaa gtgttaaatg cacaatcgcg gggaagaatg cttatgtaag 6960

gttctgttgt agtactggtg atgctatggg gatgaatatg gtttctaaag gtgtgcagaa 7020

tgttcttgag tatcttaccg atgatttccc tgacatggat gtgattggaa tctctggtaa 7080

cttctgttcg gacaagaaac ctgctgctgt gaactggatt gagggacgtg gtaaatcagt 7140

tgtttgcgag gctgtaatca gaggagagat cgtgaacaag gtcttgaaaa cgagcgtggc 7200

tgctttagtc gagctcaaca tgctcaagaa cctagctggc tctgctgttg caggctctct 7260

aggtggattc aacgctcatg ccagtaacat agtgtctgct gtattcatag ctactggcca 7320

agatccagct caaaacgtgg agagttctca atgcatcacc atgatggaag ctattaatga 7380

cggcaaagat atccatatct cagtcactat gccatctatc gaggtgggga cagtgggagg 7440

aggaacacag cttgcatctc aatcagcgtg tttaaacctg ctcggagtta aaggagcaag 7500

cacagagtcg ccgggaatga acgcaaggag gctagcgacg atcgtagccg gagcagtttt 7560

agctggagag ttatctttaa tgtcagcaat tgcagctgga cagcttgtga gaagtcacat 7620

gaaatacaat agatccagcc gagacatctc tggagcaacg acaacgacaa caacaacaac 7680

atgacccgta ggaggcacat atgagttccc aacaagagaa aaaggattat gatgaagaac 7740

aattaaggtt gatggaagaa gtttgtatcg ttgtagatga aaatgatgtc cctttaagat 7800

atggaacgaa aaaggagtgt catttgatgg aaaatataaa taaaggtctt ttgcatagag 7860

cattctctat gttcatcttt gatgagcaaa atcgcctttt acttcagcag cgtgcagaag 7920

agaaaattac atttccatcc ttatggacga atacatgttg ctcccaccca ttggatgttg 7980

ctggtgaacg tggtaatact ttacctgaag ctgttgaagg tgttaagaat gcagctcaac 8040

gcaagctgtt ccatgaattg ggtattcaag ccaagtatat tcccaaagac aaatttcagt 8100

ttcttacacg aatccattac cttgctccta gtactggtgc ttggggagag catgaaattg 8160

actacattct tttcttcaaa ggtaaagttg agctggatat caatcccaat gaagttcaag 8220

cctataagta tgttactatg gaagagttaa aagagatgtt ttccgatcct caatatggat 8280

tcacaccatg gttcaaactt atttgtgagc attttatgtt taaatggtgg caggatgtag 8340

atcatgcgtc aaaattccaa gataccttaa ttcatcgttg ctaaggatcc cccgggatcc 8400

<210> 65

<211> 55

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer containing R. capsulatus DNA

<400> 65
gcgatatcgg atccaggagg accatatgat cgccgaagcg gatatggagg tctgc 55

<210> 66

<211> 50

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer containing R. capsulatus DNA

<400> 66
gcgatatcaa gcttggatcc tcaatccatc gccaggccgc ggtcgcgcgc 50

<210> 67

<211> 60

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide containing N. tabacum and R. caopsulatus DNA

<400> 67
ctttcctgaa acataattta taatcagatc caggaggacc atatgatcgc cgaagcggat 60

<210> 68

<211> 60

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide containing N. tabacum and R. capsulatus DNA

<400> 68
cgaccgcggc ctggcgatgg attgaggatc taaacaaacc cggaacagac cgttgggaag 60

<210> 69

<211> 60

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide containing N. tabacum and R. capsulatus DNA

<400> 69
atttttcatc tcgaattgta ttcccacgaa ggccgcgtcg actacggccg caggaggagt 60

<210> 70

<211> 60

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide containing N. tabacum and R. capsulatus DNA

<400> 70
ttcggatcga tcctgcgcgg ctgagcggcc ggaatggtga agttgaaaaa cgaatccttc 60

<210> 71

<211> 1020

<212> DNA

<213> Rhodobacter capsulatus

<400> 71
atgatcgccg aagcggatat ggaggtctgc cgggagctga tccgcaccgg cagctactcc 60

ttccatgcgg cgtccagagt tctgccggcg cgggtccgtg accccgcgct ggcgctttac 120

gccttttgcc gcgtcgccga tgacgaagtc gacgaggttg gcgcgccgcg cgacaaggct 180

gcggcggttt tgaaacttgg cgaccggctg gaggacatct atgccggtcg tccgcgcaat 240

gcgccctcgg atcgggcttt cgcggcggtg gtcgaggaat tcgagatgcc gcgcgaattg 300

cccgaggcgc tgctggaggg cttcgcctgg gatgccgagg ggcggtggta tcacacgctt 360

tcggacgtgc aggcctattc ggcgcgggtg gcggccgccg tcggcgcgat gatgtgcgtg 420

ctgatgcggg tgcgcaaccc cgatgcgctg gcgcgggcct gcgatctcgg tcttgccatg 480

cagatgtcga acatcgcccg cgacgtgggc gaggatgccc gggcggggcg gcttttcctg 540

ccgaccgact ggatggtcga ggaggggatc gatccgcagg cgttcctggc cgatccgcag 600

cccaccaagg gcatccgccg ggtcaccgag cggttgctga accgcgccga ccggctttac 660

tggcgggcgg cgacgggggt gcggcttttg ccctttgact gccgaccggg gatcatggcc 720

gcgggcaaga tctatgccgc gatcggggcc gaggtggcga aggcgaaata cgacaacatc 780

acccggcgtg cccacacgac caagggccgc aagctgtggc tggtggcgaa ttccgcgatg 840

tcggcgacgg cgacctcgat gctgccgctc tcgccgcggg tgcatgccaa gcccgagccc 900

gaagtggcgc atctggtcga tgccgccgcg catcgcaacc tgcatcccga acggtccgag 960

gtgctgatct cggcgctgat ggcgctgaag gcgcgcgacc gcggcctggc gatggattga 1020

<210> 72

<211> 13917

<212> DNA

<213> Artificial Sequence

<220>

<221> misc_feature

<222> ()..()

<223> Plastid transformation vector pHKO4, containing Operon B, contain
i

<400> 72

gcacttttcg gggaaatgtg cgcggaaccc ctatttgttt atttttctaa atacattcaa 60

atatgtatcc gctcatgaga caataaccct gataaatgct tcaataatat tgaaaaagga 120

agagtatgag tattcaacat ttccgtgtcg cccttattcc ctttttttgcg gcattttgcc 180

ttcctgtttt tgctcaccca gaaacgctgg tgaaagtaaa agatgctgaa gatcagttgg 240

gtgcacgagt gggttacatc gaactggatc tcaacagcgg taagatcctt gagagttttc 300

gccccgaaga acgttttcca atgatgagca cttttaaagt tctgctatgt ggcgcggtat 360

tatcccgtat tgacgccggg caagagcaac tcggtcgccg catacactat tctcagaatg 420

acttggttga gtactcacca gtcacagaaa agcatcttac ggatggcatg acagtaagag 480

aattatgcag tgctgccata accatgagtg ataacactgc ggccaactta cttctgacaa 540

cgatcggagg accgaaggag ctaaccgctt ttttgcacaa catgggggat catgtaactc 600

gccttgatcg ttgggaaccg gagctgaatg aagccatacc aaacgacgag cgtgacacca 660

cgatgcctgt agcaatggca acaacgttgc gcaaactatt aactggcgaa ctacttactc 720

tagcttcccg gcaacaatta atagactgga tggaggcgga taaagttgca ggaccacttc 780

tgcgctcggc ccttccggct ggctggttta ttgctgataa atctggagcc ggtgagcgtg 840

ggtctcgcgg tatcattgca gcactggggc cagatggtaa gccctcccgt atcgtagtta 900

tctacacgac ggggagtcag gcaactatgg atgaacgaaa tagacagatc gctgagatag 960

gtgcctcact gattaagcat tggtaactgt cagaccaagt ttactcatat atactttaga 1020

ttgatttaaa acttcatttt taatttaaaa ggatctaggt gaagatcctt tttgataatc 1080

tcatgaccaa aatcccttaa cgtgagtttt cgttccactg agcgtcagac cccgtagaaa 1140

agatcaaagg atcttcttga gatccttttt ttctgcgcgt aatctgctgc ttgcaaacaa 1200

aaaaaccacc gctaccagcg gtggtttgtt tgccggatca agagctacca actcttttc 1260

cgaaggtaac tggcttcagc agagcgcaga taccaaatac tgtccttcta gtgtagccgt 1320

agttaggcca ccacttcaag aactctgtag caccgcctac atacctcgct ctgctaatcc 1380

tgttaccagt ggctgctgcc agtggcgata agtcgtgtct taccgggttg gactcaagac 1440

gatagttacc ggataaggcg cagcggtcgg gctgaacggg gggttcgtgc acacagccca 1500

gcttggagcg aacgacctac accgaactga gatacctaca gcgtgagcta tgagaaagcg 1560

ccacgcttcc cgaagggaga aaggcggaca ggtatccggt aagcggcagg gtcggaacag 1620

gagagcgcac gagggagctt ccagggggaa acgcctggta tctttatagt cctgtcgggt 1680

ttcgccacct ctgacttgag cgtcgatttt tgtgatgctc gtcaggggggg cggagcctat 1740

ggaaaaacgc cagcaacgcg gccttttttac ggttcctggc cttttgctgg ccttttgctc 1800

acatgttctt tcctgcgtta tcccctgatt ctgtggataa ccgtattacc gcctttgagt 1860

gagctgatac cgctcgccgc agccgaacga ccgagcgcag cgagtcagtg agcgaggaag 1920

cggaagagcg cccaatacgc aaaccgcctc tccccgcgcg ttggccgatt cattaatgca 1980

gctggcacga caggtttccc gactggaaag cgggcagtga gcgcaacgca attaatgtga 2040

gttagctcac tcattaggca ccccaggctt tacactttat gcttccggct cgtatgttgt 2100

gtggaattgt gagcggataa caatttcaca caggaaacag ctatgaccat gattacgcca 2160

agctcgaaat taaccctcac taaagggaac aaaagctgga gctccaccgc ggtggcggcc 2220

gctctagaac tagtggatct tcttggctgt tattcaaaag gtccaacaat gtatatatat 2280

tggacatttt gaggcaatta tagatcctgg aaggcaattc tgattggtca ataaaaatcg 2340

atttcaatgc tatttttttt ttgtttttta tgagtttagc caatttatca tgaaaggtaa 2400

aaggggataa aggaaccgtg tgttgattgt cctgtaaata taagttgtct tcctccatat 2460

gtaaaaaggg aataaataaa tcaattaaat ttcgggatgc ttcatgaagt gcttctttcg 2520

gagttaaact tccgtttgtc catatttcga gaaaaagtat ctcttgtttt tcattcccat 2580

tcccataaga atgaatacta tgattcgcgt ttcgaacagg catgaataca gcatctatag 2640

gataacttcc atcttgaaag ttatgtggcg tttttataag atatccacga tttctctcta 2700

tttgtaatcc aatacaaaaa tcaattggtt ccgttaaact ggctatatgt tgtgtattat 2760

caacgatttc tacataaggc ggcaagatga tatcttgggc agttacagat ccaggaccct 2820
tgacacaaat agatgcgtca gaagttccat atagattact tcttaatata atttctttca 2880
aattcattaa aatttcatgt accgattctt gaatgcccgt tatggtagaa tattcatgtg 2940
ggactttctc agattttaca cgtgtgatac atgttccttc tatttctcca agtaaagctc 3000
ttcgcatcgc aatgcctatt gtgtcggctt ggcctttcat aagtggagac agaataaagc 3060
gtccataata aaggcgttta ctgtctgttc ttgattcaac acacttccac tgtagtgtcc 3120
gagtagatac tgttactttc tctcgaacca tagtactatt atttgattag atcatcgaat 3180
cttttatttc tcttgagatt tcttcaatgt tcagttctac acacgtcttt ttttcggagg 3240
tctacagcca ttatgtggca taggagttac atcccgtacg aaagttaata gtataccact 3300
tcgacgaata gctcgtaatg ctgcatctct tccgagaccg ggacctttta tcatgacttc 3360
tgctcgttgc ataccttgat ccactactgt acggatagcg tttgctgctg cggtttgagc 3420
agcaaacggt gttcctcttc tcgtaccttt gaatccagaa gtaccggcgg aggaccaaga 3480
aactactcga ccccgtacat ctgtaacagt gacaatggta ttattgaaac ttgcttgaac 3540
atgaataact ccctttggta ttctacgtgc acccttacgt gaaccaatac gtccattcct 3600
acgcgaacta attttcggta tagcttttgc catattttat catctcgtaa atatgagtca 3660
gagatatatg gatatatcca tttcatgtca aaacagattc tttatttgta catcggctct 3720
tctggcaagt ctgattatcc ctgtctttgt ttatgtctcg ggttggaaca aattactata 3780
attcgtcccc gcctacggat tagtcgacat ttttcacaaa ttttacgaac ggaagctctt 3840
attttcatat ttctcattcc ttaccttaat tctgaatcta tttcttggaa gaaaataagt 3900
ttcttgaaat ttttcatctc gaattgtatt cccacgaaag gaatggtgaa gttgaaaaac 3960
gaatccttca aatctttgtt gtggagtcga taaattatac gccctttggt tgaatcataa 4020
ggacttactt caattttgac tctatctcct ggcagtatcc gtataaaact atgccggatc 4080
tttcctgaaa cataatttat aatcagatcg gccgcaggag gagttcatat gtcagagttg 4140
agagccttca gtgccccagg gaaagcgtta ctagctggtg gatatttagt tttagataca 4200
aaatatgaag catttgtagt cggattatcg gcaagaatgc atgctgtagc ccatccttac 4260
ggttcattgc aagggtctga taagtttgaa gtgcgtgtga aaagtaaaca atttaaagat 4320
ggggagtggc tgtaccatat aagtcctaaa agtggcttca ttcctgtttc gataggcgga 4380
tctaagaacc ctttcattga aaaagttatc gctaacgtat ttagctactt taaacctaac 4440
atggacgact actgcaatag aaacttgttc gttattgata ttttctctga tgatgcctac 4500
cattctcagg aggatagcgt taccgaacat cgtggcaaca gaagattgag ttttcattcg 4560
cacagaattg aagaagttcc caaaacaggg ctgggctcct cggcaggttt agtcacagtt 4620
ttaactacag ctttggcctc ctttttttgta tcggacctgg aaaataatgt agacaaatat 4680

agagaagtta ttcataattt agcacaagtt gctcattgtc aagctcaggg taaaattgga 4740
agcgggtttg atgtagcggc ggcagcatat ggatctatca gatatagaag attcccaccc 4800
gcattaatct ctaatttgcc agatattgga agtgctactt acggcagtaa actggcgcat 4860
ttggttgatg aagaagactg gaatattacg attaaaagta accatttacc ttcgggatta 4920
actttatgga tgggcgatat taagaatggt tcagaaacag taaaactggt ccagaaggta 4980
aaaaattggt atgattcgca tatgccagaa agcttgaaaa tatatacaga actcgatcat 5040
gcaaattcta gatttatgga tggactatct aaactagatc gcttacacga gactcatgac 5100
gattacagcg atcagatatt tgagtctctt gagaggaatg actgtacctg tcaaaagtat 5160
cctgaaatca cagaagttag agatgcagtt gccacaatta gacgttcctt tagaaaaata 5220
actaaagaat ctggtgccga tatcgaacct cccgtacaaa ctagcttatt ggatgattgc 5280
cagaccttaa aaggagttct tacttgctta atacctggtg ctggtggtta tgacgccatt 5340
gcagtgatta ctaagcaaga tgttgatctt agggctcaaa ccgctaatga caaaagattt 5400
tctaaggttc aatggctgga tgtaactcag gctgactggg gtgttaggaa agaaaaagat 5460
ccggaaactt atcttgataa actgcaggag gagttttaat gtcattaccg ttcttaactt 5520
ctgcaccggg aaaggttatt atttttggtg aacactctgc tgtgtacaac aagcctgccg 5580
tcgctgctag tgtgtctgcg ttgagaacct acctgctaat aagcgagtca tctgcaccag 5640
atactattga attggacttc ccggacatta gctttaatca taagtggtcc atcaatgatt 5700
tcaatgccat caccgaggat caagtaaact cccaaaaatt ggccaaggct caacaagcca 5760
ccgatggctt gtctcaggaa ctcgttagtc ttttggatcc gttgttagct caactatccg 5820
aatccttcca ctaccatgca gcgttttgtt tcctgtatat gtttgtttgc ctatgccccc 5880
atgccaagaa tattaagttt tctttaaagt ctactttacc catcggtgct gggttgggct 5940
caagcgcctc tatttctgta tcactggcct tagctatggc ctacttgggg gggttaatag 6000
gatctaatga cttggaaaag ctgtcagaaa acgataagca tatagtgaat caatgggcct 6060
tcataggtga aaagtgtatt cacggtaccc cttcaggaat agataacgct gtggccactt 6120
atggtaatgc cctgctattt gaaaaagact cacataatgg aacaataaac acaaacaatt 6180
ttaagttctt agatgatttc ccagccattc caatgatcct aacctatact agaattccaa 6240
ggtctacaaa agatcttgtt gctcgcgttc gtgtgttggt caccgagaaa tttcctgaag 6300
ttatgaagcc aattctagat gccatgggtg aatgtgccct acaaggctta gagatcatga 6360
ctaagttaag taaatgtaaa ggcaccgatg acgaggctgt agaaactaat aatgaactgt 6420
atgaacaact attggaattg ataagaataa atcatggact gcttgtctca atcggtgttt 6480
ctcatcctgg attagaactt attaaaaatc tgagcgatga tttgagaatt ggctccacaa 6540
aacttaccgg tgctggtggc ggcggttgct ctttgacttt gttacgaaga gacattactc 6600

aagagcaaat tgacagcttc aaaaagaaat tgcaagatga ttttagttac gagacatttg 6660

aaacagactt gggtgggact ggctgctgtt tgttaagcgc aaaaaatttg aataaagatc 6720

ttaaaatcaa atccctagta ttccaattat ttgaaaataa aactaccaca aagcaacaaa 6780

ttgacgatct attattgcca ggaaacacga atttaccatg gacttcagac gaggagtttt 6840

aatgactgta tatactgcta gtgtaactgc tccggtaaat attgctactc ttaagtattg 6900

ggggaaaagg gacacgaagt tgaatctgcc caccaattcg tccatatcag tgactttatc 6960

gcaagatgac ctcagaacgt tgacctctgc ggctactgca cctgagtttg aacgcgacac 7020

tttgtggtta aatggagaac cacacagcat cgacaatgaa agaactcaaa attgtctgcg 7080

cgacctacgc caattaagaa aggaaatgga atcgaaggac gcctcattgc ccacattatc 7140

tcaatggaaa ctccacattg tctccgaaaa taactttcct acagcagctg gtttagcttc 7200

ctccgctgct ggctttgctg cattggtctc tgcaattgct aagttatacc aattaccaca 7260

gtcaacttca gaaatatcta gaatagcaag aaaggggtct ggttcagctt gtagatcgtt 7320

gtttggcgga tacgtggcct gggaaatggg aaaagctgaa gatggtcatg attccatggc 7380

agtacaaatc gcagacagct ctgactggcc tcagatgaaa gcttgtgtcc tagttgtcag 7440

cgatattaaa aaggatgtga gttccactca gggtatgcaa ttgaccgtgg caacctccga 7500

actatttaaa gaaagaattg aacatgtcgt accaaagaga tttgaagtca tgcgtaaagc 7560

cattgttgaa aaagatttcg ccacctttgc aaaggaaaca atgatggatt ccaactcttt 7620

ccatgccaca tgtttggact ctttccctcc aatattctac atgaatgaca cttccaagcg 7680

tatcatcagt tggtgccaca ccattaatca gttttacgga gaaacaatcg ttgcatacac 7740

gtttgatgca ggtccaaatg ctgtgttgta ctacttagct gaaaatgagt cgaaactctt 7800

tgcatttatc tataaattgt ttggctctgt tcctggatgg gacaagaaat ttactactga 7860

gcagcttgag gctttcaacc atcaatttga atcatctaac tttactgcac gtgaattgga 7920

tcttgagttg caaaaggatg ttgccagagt gattttaact caagtcggtt caggcccaca 7980

agaaacaaac gaatctttga ttgacgcaaa gactggtcta ccaaaggaag aggagtttta 8040

actcgacgcc ggcggaggca catatgtctc agaacgttta cattgtatcg actgccagaa 8100

ccccaattgg ttcattccag ggttctctat cctccaagac agcagtggaa ttgggtgctg 8160

ttgctttaaa aggcgccttg gctaaggttc cagaattgga tgcatccaag gattttgacg 8220

aaattatttt tggtaacgtt ctttctgcca atttgggcca agctccggcc agacaagttg 8280

ctttggctgc cggtttgagt aatcatatcg ttgcaagcac agttaacaag gtctgtgcat 8340

ccgctatgaa ggcaatcatt ttgggtgctc aatccatcaa atgtggtaat gctgatgttg 8400

tcgtagctgg tggttgtgaa tctatgacta acgcaccata ctacatgcca gcagcccgtg 8460

cgggtgccaa atttggccaa actgttcttg ttgatggtgt cgaaagagat gggttgaacg 8520

atgcgtacga tggtctagcc atgggtgtac acgcagaaaa gtgtgcccgt gattgggata 8580
ttactagaga acaacaagac aattttgcca tcgaatccta ccaaaaatct caaaaatctc 8640
aaaaggaagg taaattcgac aatgaaattg tacctgttac cattaaggga tttagaggta 8700
agcctgatac tcaagtcacg aaggacgagg aacctgctag attacacgtt gaaaaattga 8760
gatctgcaag gactgttttc caaaaagaaa acggtactgt tactgccgct aacgcttctc 8820
caatcaacga tggtgctgca gccgtcatct tggtttccga aaaagttttg aaggaaaaga 8880
atttgaagcc tttggctatt atcaaaggtt ggggtgaggc cgctcatcaa ccagctgatt 8940
ttacatgggc tccatctctt gcagttccaa aggctttgaa acatgctggc atcgaagaca 9000
tcaattctgt tgattacttt gaattcaatg aagccttttc ggttgtcggt ttggtgaaca 9060
ctaagatttt gaagctagac ccatctaagg ttaatgtata tggtggtgct gttgctctag 9120
gtcacccatt gggttgttct ggtgctagag tggttgttac actgctatcc atcttacagc 9180
aagaaggagg taagatcggt gttgccgcca tttgtaatgg tggtggtggt gcttcctcta 9240
ttgtcattga aaagatatga ggatcctcta gatgcgcagg aggcacatat ggcgaagaac 9300
gttgggattt tggctatgga tatctatttc cctcccacct gtgttcaaca ggaagctttg 9360
gaagcacatg atggagcaag taaagggaaa tacactattg gacttggcca agattgttta 9420
gctttttgca ctgagcttga agatgttatc tctatgagtt tcaatgcggt gacatcactt 9480
tttgagaagt ataagattga ccctaaccaa atcgggcgtc ttgaagtagg aagtgagact 9540
gttattgaca aaagcaagtc catcaagacc ttcttgatgc agctctttga gaaatgtgga 9600
aacactgatg tcgaaggtgt tgactcgacc aatgcttgct atggtggaac tgcagctttg 9660
ttaaactgtg tcaattgggt tgagagtaac tcttgggatg gacgttatgg cctcgtcatt 9720
tgtactgaca gcgcggttta tgcagaagga cccgcaaggc ccactggagg agctgcagcg 9780
attgctatgt tgataggacc tgatgctcct atcgttttcg aaagcaaatt gagagcaagc 9840
cacatggctc atgtctatga cttttacaag cccaatcttg ctagcgagta cccggttgtt 9900
gatggtaagc tttcacagac ttgctacctc atggctcttg actcctgcta taaacattta 9960
tgcaacaagt tcgagaagat cgagggcaaa gagttctcca taaatgatgc tgattacatt 10020
gttttccatt ctccatacaa taaacttgta cagaaaagct ttgctcgtct cttgtacaac 10080
gacttcttga gaaacgcaag ctccattgac gaggctgcca aagaaaagtt caccccttat 10140
tcatctttga cccttgacga gagttaccaa agccgtgatc ttgaaaaggt gtcacaacaa 10200
atttcgaaac cgttttatga tgctaaagtg caaccaacga ctttaatacc aaaggaagtc 10260
ggtaacatgt acactgcttc tctctacgct gcatttgctt ccctcatcca caataaacac 10320
aatgatttgg cgggaaagcg ggtggttatg ttctcttatg gaagtggctc caccgcaaca 10380
atgttctcat tacgcctcaa cgacaataag cctcctttca gcatttcaaa cattgcatct 10440

gtaatggatg ttggcggtaa attgaaagct agacatgagt atgcacctga gaagtttgtg 10500
gagacaatga agctaatgga acataggtat ggagcaaagg actttgtgac aaccaaggag 10560
ggtattatag atcttttggc accgggaact tattatctga aagaggttga ttccttgtac 10620
cggagattct atggcaagaa aggtgaagat ggatctgtag ccaatggaca ctgaggatcc 10680
gtcgagcacg tggaggcaca tatgcaatgc tgtgagatgc ctgttggata cattcagatt 10740
cctgttggga ttgctggtcc attgttgctt gatggttatg agtactctgt tcctatggct 10800
acaaccgaag gttgtttggt tgctagcact aacagaggct gcaaggctat gtttatctct 10860
ggtggcgcca ccagtaccgt tcttaaggac ggtatgaccc gagcacctgt tgttcggttc 10920
gcttcggcga gacgagcttc ggagcttaag tttttcttgg agaatccaga gaactttgat 10980
actttggcag tagtcttcaa caggtcgagt agatttgcaa gactgcaaag tgttaaatgc 11040
acaatcgcgg ggaagaatgc ttatgtaagg ttctgttgta gtactggtga tgctatgggg 11100
atgaatatgg tttctaaagg tgtgcagaat gttcttgagt atcttaccga tgatttccct 11160
gacatggatg tgattggaat ctctggtaac ttctgttcgg acaagaaacc tgctgctgtg 11220
aactggattg agggacgtgg taaatcagtt gtttgcgagg ctgtaatcag aggagagatc 11280
gtgaacaagg tcttgaaaac gagcgtggct gctttagtcg agctcaacat gctcaagaac 11340
ctagctggct ctgctgttgc aggctctcta ggtggattca acgctcatgc cagtaacata 11400
gtgtctgctg tattcatagc tactggccaa gatccagctc aaaacgtgga gagttctcaa 11460
tgcatcacca tgatggaagc tattaatgac ggcaaagata tccatatctc agtcactatg 11520
ccatctatcg aggtggggac agtgggagga ggaacacagc ttgcatctca atcagcgtgt 11580
ttaaacctgc tcggagttaa aggagcaagc acagagtcgc cgggaatgaa cgcaaggagg 11640
ctagcgacga tcgtagccgg agcagtttta gctggagagt tatctttaat gtcagcaatt 11700
gcagctggac agcttgtgag aagtcacatg aaatacaata gatccagccg agacatctct 11760
ggagcaacga caacgacaac aacaacaaca tgacccggga tccggccgat ctaaacaaac 11820
ccggaacaga ccgttgggaa gcgattcagt aattaaagct tcatgactcc tttttggttc 11880
ttaaagtccc tttgaggtat caactaataa gaaagatatt agacaacccc ccttttttct 11940
ttttcacaaa taggaagttt cgaatccaat ttggatatta aaaggattac cagatataac 12000
acaaaatctc tccacctatt ccttctagtc gagcctctcg gtctgtcatt atacctcgag 12060
aagtagaaag aattacaatc cccattccac ctaaaattcg cggaattcgt tgataattag 12120
aatagattcg tagaccaggt cgactgattc gttttaaatt taaaatattt ctatagggtc 12180
ttttcctatt ccttctatgt cgcagggtta aaaccaaaaa atatttgttt ttttctcgat 12240
gttttctcac gttttcgata aaaccttctc gtaaaagtat ttgaacaata ttttcggtaa 12300
tattagtaga tgctattcga accacccttt ttcgatccat atcagcattt cgtatagaag 12360

ttattatctc agcaatagtg tccctaccca tgatgaacta aaattattgg ggcctccaaa 12420
tttgatataa tcaacgtgtt ttttacttat ttttttttg aatatgatat gaattattaa 12480
agatatatgc gtgagacaca atctactaat taatctattt ctttcaaata ccccactaga 12540
aacagatcac aatttcattt tataatacct cgggagctaa tgaaactatt ttagtaaaat 12600
ttaattctct caattcccgg gcgattgcac caaaaattcg agttcctttt gatttccttc 12660
cttcttgatc aataacaact gcagcattgt catcatatcg tattatcatc ccgttgtcac 12720
gtttgagttc tttacaggtc cgcacaatta cagctctgac tacttctgat ctttctaggg 12780
gcatatttgg tacggcttct ttgatcacag caacaataac gtcaccaata tgagcatatc 12840
gacgattgct agctcctatg attcgaatac acatcaattc tcgagccccg ctgttatccg 12900
ctacatttaa atgggtctga ggttgaatca ttttttttaat ccgttctttg aatgcaaagg 12960
gcgaagaaaa aaaagaaata tttttgtcca aaaaaaaaga aacatgcggt ttcgtttcat 13020
atctaagagc cctttccgca tttttttcta ttacattacg aaataatgaa ttgagttcgt 13080
ataggcattt tagatgctgc tagtgaaata gcccttctgg ctatattttc tgttactcca 13140
cccatttcat aaagtattcg acccggttta acaacagcta cccaatattc aggggatccc 13200
ccgggctgca ggaattcgat atcaagctta tcgataccgt cgacctcgag gggggcccg 13260
gtacccaatt cgccctatag tgagtcgtat tacaattcac tggccgtcgt tttacaacgt 13320
cgtgactggg aaaaccctgg cgttacccaa cttaatcgcc ttgcagcaca tccccctttc 13380
gccagctggc gtaatagcga agaggcccgc accgatcgcc cttcccaaca gttgcgcagc 13440
ctgaatggcg aatgggacgc gccctgtagc ggcgcattaa gcgcggcggg tgtggtggtt 13500
acgcgcagcg tgaccgctac acttgccagc gccctagcgc ccgctccttt cgctttcttc 13560
ccttcctttc tcgccacgtt cgccggcttt ccccgtcaag ctctaaatcg ggggctccct 13620
ttagggttcc gatttagtgc tttacggcac ctcgacccca aaaaacttga ttagggtgat 13680
ggttcacgta gtgggccatc gccctgatag acggtttttc gccctttgac gttggagtcc 13740
acgttcttta atagtggact cttgttccaa actggaacaa cactcaaccc tatctcggtc 13800
tattcttttg atttataagg gattttgccg atttcggcct attggttaaa aaatgagctg 13860
atttaacaaa aatttaacgc gaattttaac aaaatattaa cgcttacaat ttaggtg 13917

<210> 73

<211> 7252

<212> DNA

<213> Artificial Sequence

<220>

<221> misc_feature

<222> ()..()

<223> Plastid transformation vector pHK07, containing Operon C, contain
i

<400> 73

gcacttttcg gggaaatgtg cgcggaaccc ctatttgttt atttttctaa atacattcaa 60

atatgtatcc gctcatgaga caataaccct gataaatgct tcaataatat tgaaaaagga 120

agagtatgag tattcaacat ttccgtgtcg cccttattcc ctttttttgcg gcattttgcc 180

ttcctgtttt tgctcaccca gaaacgctgg tgaaagtaaa agatgctgaa gatcagttgg 240

gtgcacgagt gggttacatc gaactggatc tcaacagcgg taagatcctt gagagttttc 300

gccccgaaga acgttttcca atgatgagca cttttaaagt tctgctatgt ggcgcggtat 360

tatcccgtat tgacgccggg caagagcaac tcggtcgccg catacactat tctcagaatg 420

acttggttga gtactcacca gtcacagaaa agcatcttac ggatggcatg acagtaagag 480

aattatgcag tgctgccata accatgagtg ataacactgc ggccaactta cttctgacaa 540

cgatcggagg accgaaggag ctaaccgctt ttttgcacaa catgggggat catgtaactc 600

gccttgatcg ttgggaaccg gagctgaatg aagccatacc aaacgacgag cgtgacacca 660

cgatgcctgt agcaatggca acaacgttgc gcaaactatt aactggcgaa ctacttactc 720

tagcttcccg gcaacaatta atagactgga tggaggcgga taaagttgca ggaccacttc 780

tgcgctcggc ccttccggct ggctggttta ttgctgataa atctggagcc ggtgagcgtg 840

ggtctcgcgg tatcattgca gcactggggc cagatggtaa gccctcccgt atcgtagtta 900

tctacacgac ggggagtcag gcaactatgg atgaacgaaa tagacagatc gctgagatag 960

gtgcctcact gattaagcat tggtaactgt cagaccaagt ttactcatat atactttaga 1020

ttgatttaaa acttcatttt taatttaaaa ggatctaggt gaagatcctt tttgataatc 1080

tcatgaccaa aatcccttaa cgtgagtttt cgttccactg agcgtcagac cccgtagaaa 1140

agatcaaagg atcttcttga gatccttttt ttctgcgcgt aatctgctgc ttgcaaacaa 1200

aaaaaccacc gctaccagcg gtggtttgtt tgccggatca agagctacca actcttttc 1260

cgaaggtaac tggcttcagc agagcgcaga taccaaatac tgtccttcta gtgtagccgt 1320

agttaggcca ccacttcaag aactctgtag caccgcctac atacctcgct ctgctaatcc 1380

tgttaccagt ggctgctgcc agtggcgata agtcgtgtct taccgggttg gactcaagac 1440

gatagttacc ggataaggcg cagcggtcgg gctgaacggg gggttcgtgc acacagccca 1500

gcttggagcg aacgacctac accgaactga gatacctaca gcgtgagcta tgagaaagcg 1560

ccacgcttcc cgaagggaga aaggcggaca ggtatccggt aagcggcagg gtcggaacag 1620

gagagcgcac gagggagctt ccagggggaa acgcctggta tctttatagt cctgtcgggt 1680

ttcgccacct ctgacttgag cgtcgatttt tgtgatgctc gtcaggggggg cggagcctat 1740

ggaaaaacgc cagcaacgcg gccttttttac ggttcctggc cttttgctgg ccttttgctc 1800

acatgttctt tcctgcgtta tcccctgatt ctgtggataa ccgtattacc gcctttgagt 1860

gagctgatac cgctcgccgc agccgaacga ccgagcgcag cgagtcagtg agcgaggaag 1920

cggaagagcg cccaatacgc aaaccgcctc tccccgcgcg ttggccgatt cattaatgca 1980

gctggcacga caggtttccc gactggaaag cgggcagtga gcgcaacgca attaatgtga 2040

gttagctcac tcattaggca ccccaggctt tacactttat gcttccggct cgtatgttgt 2100

gtggaattgt gagcggataa caatttcaca caggaaacag ctatgaccat gattacgcca 2160

agctcgaaat taaccctcac taaagggaac aaaagctgga gctccaccgc ggtggcggcc 2220

gctctagaac tagtggatct tcttggctgt tattcaaaag gtccaacaat gtatatatat 2280

tggacatttt gaggcaatta tagatcctgg aaggcaattc tgattggtca ataaaaatcg 2340

atttcaatgc tatttttttt ttgtttttta tgagtttagc caatttatca tgaaaggtaa 2400

aaggggataa aggaaccgtg tgttgattgt cctgtaaata taagttgtct tcctccatat 2460

gtaaaaaggg aataaataaa tcaattaaat ttcgggatgc ttcatgaagt gcttctttcg 2520

gagttaaact tccgtttgtc catatttcga gaaaaagtat ctcttgtttt tcattcccat 2580

tcccataaga atgaatacta tgattcgcgt ttcgaacagg catgaataca gcatctatag 2640

gataacttcc atcttgaaag ttatgtggcg tttttataag atatccacga tttctctcta 2700

tttgtaatcc aatacaaaaa tcaattggtt ccgttaaact ggctatatgt tgtgtattat 2760

caacgatttc tacataaggc ggcaagatga tatcttgggc agttacagat ccaggaccct 2820

tgacacaaat agatgcgtca gaagttccat atagattact tcttaatata atttctttca 2880

aattcattaa aatttcatgt accgattctt gaatgcccgt tatggtagaa tattcatgtg 2940

ggactttctc agattttaca cgtgtgatac atgttccttc tatttctcca agtaaagctc 3000

ttcgcatcgc aatgcctatt gtgtcggctt ggcctttcat aagtggagac agaataaagc 3060

gtccataata aaggcgttta ctgtctgttc ttgattcaac acacttccac tgtagtgtcc 3120

gagtagatac tgttactttc tctcgaacca tagtactatt atttgattag atcatcgaat 3180

cttttatttc tcttgagatt tcttcaatgt tcagttctac acacgtcttt ttttcggagg 3240

tctacagcca ttatgtggca taggagttac atcccgtacg aaagttaata gtataccact 3300

tcgacgaata gctcgtaatg ctgcatctct tccgagaccg ggacctttta tcatgacttc 3360

tgctcgttgc ataccttgat ccactactgt acggatagcg tttgctgctg cggtttgagc 3420
agcaaacggt gttcctcttc tcgtaccttt gaatccagaa gtaccggcgg aggaccaaga 3480
aactactcga ccccgtacat ctgtaacagt gacaatggta ttattgaaac ttgcttgaac 3540
atgaataact ccctttggta ttctacgtgc acccttacgt gaaccaatac gtccattcct 3600
acgcgaacta attttcggta tagcttttgc catattttat catctcgtaa atatgagtca 3660
gagatatatg gatatatcca tttcatgtca aaacagattc tttatttgta catcggctct 3720
tctggcaagt ctgattatcc ctgtctttgt ttatgtctcg ggttggaaca aattactata 3780
attcgtcccc gcctacggat tagtcgacat ttttcacaaa ttttacgaac ggaagctctt 3840
attttcatat ttctcattcc ttaccttaat tctgaatcta tttcttggaa gaaaataagt 3900
ttcttgaaat ttttcatctc gaattgtatt cccacgaaag gaatggtgaa gttgaaaaac 3960
gaatccttca aatctttgtt gtggagtcga taaattatac gccctttggt tgaatcataa 4020
ggacttactt caattttgac tctatctcct ggcagtatcc gtataaaact atgccggatc 4080
tttcctgaaa cataatttat aatcagatcc aggaggacca tatgatcgcc gaagcggata 4140
tggaggtctg ccgggagctg atccgcaccg gcagctactc cttccatgcg gcgtccagag 4200
ttctgccggc gcgggtccgt gaccccgcgc tggcgcttta cgcctttgc cgcgtcgccg 4260
atgacgaagt cgacgaggtt ggcgcgccgc gcgacaaggc tgcggcggtt ttgaaacttg 4320
gcgaccggct ggaggacatc tatgccggtc gtccgcgcaa tgcgccctcg gatcgggctt 4380
tcgcggcggt ggtcgaggaa ttcgagatgc cgcgcgaatt gcccgaggcg ctgctggagg 4440
gcttcgcctg ggatgccgag gggcggtggt atcacacgct ttcggacgtg caggcctatt 4500
cggcgcgggt ggcggccgcc gtcggcgcga tgatgtgcgt gctgatgcgg gtgcgcaacc 4560
ccgatgcgct ggcgcgggcc tgcgatctcg gtcttgccat gcagatgtcg aacatcgccc 4620
gcgacgtggg cgaggatgcc cgggcggggc ggcttttcct gccgaccgac tggatggtcg 4680
aggaggggat cgatccgcag gcgttcctgg ccgatccgca gcccaccaag ggcatccgcc 4740
gggtcaccga gcggttgctg aaccgcgccg accggcttta ctggcgggcg gcgacggggg 4800
tgcggctttt gcccttgac tgccgaccgg ggatcatggc cgcgggcaag atctatgccg 4860
cgatcggggc cgaggtggcg aaggcgaaat acgacaacat cacccggcgt gcccacacga 4920
ccaagggccg caagctgtgg ctggtggcga attccgcgat gtcggcgacg gcgacctcga 4980
tgctgccgct ctcgccgcgg gtgcatgcca agcccgagcc cgaagtggcg catctggtcg 5040
atgccgccgc gcatcgcaac ctgcatcccg aacggtccga ggtgctgatc tcggcgctga 5100
tggcgctgaa ggcgcgcgac cgcggcctgg cgatggattg aggatctaaa caaacccgga 5160
acagaccgtt gggaagcgat tcagtaatta aagcttcatg actccttttt ggttcttaaa 5220
gtcccttga ggtatcaact aataagaaag atattagaca acccccctt tttcttttc 5280

acaaatagga agtttcgaat ccaatttgga tattaaaagg attaccagat ataacacaaa 5340
atctctccac ctattccttc tagtcgagcc tctcggtctg tcattatacc tcgagaagta 5400
gaaagaatta caatccccat tccacctaaa attcgcggaa ttcgttgata attagaatag 5460
attcgtagac caggtcgact gattcgtttt aaatttaaaa tatttctata gggtcttttc 5520
ctattccttc tatgtcgcag ggttaaaacc aaaaaatatt tgtttttttc tcgatgtttt 5580
ctcacgtttt cgataaaacc ttctcgtaaa agtatttgaa caatattttc ggtaatatta 5640
gtagatgcta ttcgaaccac ccttttcga tccatatcag catttcgtat agaagttatt 5700
atctcagcaa tagtgtccct acccatgatg aactaaaatt attggggcct ccaaatttga 5760
tataatcaac gtgtttttta cttatttttt ttttgaatat gatatgaatt attaaagata 5820
tatgcgtgag acacaatcta ctaattaatc tatttctttc aaatacccca ctagaaacag 5880
atcacaattt cattttataa tacctcggga gctaatgaaa ctattttagt aaaatttaat 5940
tctctcaatt cccgggcgat tgcaccaaaa attcgagttc cttttgattt ccttccttct 6000
tgatcaataa caactgcagc attgtcatca tatcgtatta tcatcccgtt gtcacgtttg 6060
agttctttac aggtccgcac aattacagct ctgactactt ctgatctttc taggggcata 6120
tttggtacgg cttctttgat cacagcaaca ataacgtcac caatatgagc atatcgacga 6180
ttgctagctc ctatgattcg aatacacatc aattctcgag ccccgctgtt atccgctaca 6240
tttaaatggg tctgaggttg aatcattttt ttaatccgtt ctttgaatgc aaagggcgaa 6300
gaaaaaaaag aaatattttt gtccaaaaaa aaagaaacat gcggtttcgt ttcatatcta 6360
agagcccttt ccgcattttt ttctattaca ttacgaaata atgaattgag ttcgtatagg 6420
cattttagat gctgctagtg aaatagccct tctggctata ttttctgtta ctccacccat 6480
ttcataaagt attcgacccg gtttaacaac agctacccaa tattcagggg atcccccggg 6540
ctgcaggaat tcgatatcaa gcttatcgat accgtcgacc tcgaggggggg gcccggtacc 6600
caattcgccc tatagtgagt cgtattacaa ttcactggcc gtcgttttac aacgtcgtga 6660
ctgggaaaac cctggcgtta cccaacttaa tcgccttgca gcacatcccc ctttcgccag 6720
ctggcgtaat agcgaagagg cccgcaccga tcgcccttcc caacagttgc gcagcctgaa 6780
tggcgaatgg gacgcgccct gtagcggcgc attaagcgcg gcgggtgtgg tggttacgcg 6840
cagcgtgacc gctacacttg ccagcgccct agcgcccgct cctttcgctt tcttcccttc 6900
ctttctcgcc acgttcgccg gctttccccg tcaagctcta aatcgggggc tcccttttagg 6960
gttccgattt agtgctttac ggcacctcga ccccaaaaaa cttgattagg gtgatggttc 7020
acgtagtggg ccatcgccct gatagacggt ttttcgccct ttgacgttgg agtccacgtt 7080
ctttaatagt ggactcttgt tccaaactgg aacaacactc aaccctatct cggtctattc 7140
ttttgattta taagggattt tgccgatttc ggcctattgg ttaaaaaatg agctgattta 7200

acaaaaattt aacgcgaatt ttaacaaaat attaacgctt acaatttagg tg 7252

<210> 74

<211> 14623

<212> DNA

<213> Artificial Sequence

<220>

<221> misc_feature

<222> ()..()

<223> Plastic transformation vector pHKO8, containing Operon G, contain
i

<400> 74

cacctaaatt gtaagcgtta atattttgtt aaaattcgcg ttaaattttt gttaaatcag 60

ctcatttttt aaccaatagg ccgaaatcgg caaaatccct tataaatcaa aagaatagac 120

cgagataggg ttgagtgttg ttccagtttg gaacaagagt ccactattaa agaacgtgga 180

ctccaacgtc aaagggcgaa aaaccgtcta tcagggcgat ggcccactac gtgaaccatc 240

accctaatca agtttttttgg ggtcgaggtg ccgtaaagca ctaaatcgga accctaaagg 300

gagcccccga tttagagctt gacggggaaa gccggcgaac gtggcgagaa aggaagggaa 360

gaaagcgaaa ggagcgggcg ctagggcgct ggcaagtgta gcggtcacgc tgcgcgtaac 420

caccacaccc gccgcgctta atgcgccgct acagggcgcg tcccattcgc cattcaggct 480

gcgcaactgt tgggaagggc gatcggtgcg ggcctcttcg ctattacgcc agctggcgaa 540

aggggatgt gctgcaaggc gattaagttg ggtaacgcca gggttttccc agtcacgacg 600

ttgtaaaacg acggccagtg aattgtaata cgactcacta tagggcgaat tgggtaccgg 660

gccccccctc gaggtcgacg gtatcgataa gcttgatatc gaattcctgc agcccgggggg 720

atcttcttgg ctgttattca aaaggtccaa caatgtatat atattggaca ttttgaggca 780

attatagatc ctggaaggca attctgattg gtcaataaaa atcgatttca atgctatttt 840

ttttttgttt tttatgagtt tagccaattt atcatgaaag gtaaaagggg ataaaggaac 900

cgtgtgttga ttgtcctgta aatataagtt gtcttcctcc atatgtaaaa agggaataaa 960

taaatcaatt aaatttcggg atgcttcatg aagtgcttct ttcggagtta aacttccgtt 1020

tgtccatatt tcgagaaaaa gtatctcttg tttttcattc ccattcccat aagaatgaat 1080

actatgattc gcgtttcgaa caggcatgaa tacagcatct ataggataac ttccatcttg 1140
aaagttatgt ggcgttttta taagatatcc acgatttctc tctatttgta atccaataca 1200
aaaatcaatt ggttccgtta aactggctat atgttgtgta ttatcaacga tttctacata 1260
aggcggcaag atgatatctt gggcagttac agatccagga cccttgacac aaatagatgc 1320
gtcagaagtt ccatatagat tacttcttaa tataatttct ttcaaattca ttaaaatttc 1380
atgtaccgat tcttgaatgc ccgttatggt agaatattca tgtgggactt tctcagattt 1440
tacacgtgtg atacatgttc cttctatttc tccaagtaaa gctcttcgca tcgcaatgcc 1500
tattgtgtcg gcttggcctt tcataagtgg agacagaata aagcgtccat aataaaggcg 1560
tttactgtct gttcttgatt caacacactt ccactgtagt gtccgagtag atactgttac 1620
tttctctcga accatagtac tattatttga ttagatcatc gaatctttta tttctcttga 1680
gatttcttca atgttcagtt ctacacacgt ctttttttcg gaggtctaca gccattatgt 1740
ggcataggag ttacatcccg tacgaaagtt aatagtatac cacttcgacg aatagctcgt 1800
aatgctgcat ctcttccgag accgggacct tttatcatga cttctgctcg ttgcatacct 1860
tgatccacta ctgtacggat agcgtttgct gctgcggttt gagcagcaaa cggtgttcct 1920
cttctcgtac ctttgaatcc agaagtaccg gcggaggacc aagaaactac tcgaccccgt 1980
acatctgtaa cagtgacaat ggtattattg aaacttgctt gaacatgaat aactcccttt 2040
ggtattctac gtgcaccctt acgtgaacca atacgtccat tcctacgcga actaattttc 2100
ggtatagctt ttgccatatt ttatcatctc gtaaatatga gtcagagata tatggatata 2160
tccatttcat gtcaaaacag attctttatt tgtacatcgg ctcttctggc aagtctgatt 2220
atccctgtct ttgtttatgt ctcgggttgg aacaaattac tataattcgt ccccgcctac 2280
ggattagtcg acatttttca caaattttac gaacggaagc tcttattttc atatttctca 2340
ttccttacct taattctgaa tctatttctt ggaagaaaat aagtttcttg aaatttttca 2400
tctcgaattg tattcccacg aaaggaatgg tgaagttgaa aaacgaatcc ttcaaatctt 2460
tgttgtggag tcgataaatt atacgccctt tggttgaatc ataaggactt acttcaattt 2520
tgactctatc tcctggcagt atccgtataa aactatgccg gatctttcct gaaacataat 2580
ttataatcag atcggccgca ggaggagttc atatgtcaga gttgagagcc ttcagtgccc 2640
cagggaaagc gttactagct ggtggatatt tagttttaga tacaaaatat gaagcatttg 2700
tagtcggatt atcggcaaga atgcatgctg tagcccatcc ttacggttca ttgcaagggt 2760
ctgataagtt tgaagtgcgt gtgaaaagta aacaatttaa agatggggag tggctgtacc 2820
atataagtcc taaaagtggc ttcattcctg tttcgatagg cggatctaag aacccttttca 2880
ttgaaaaagt tatcgctaac gtatttagct actttaaacc taacatggac gactactgca 2940
atagaaactt gttcgttatt gatattttct ctgatgatgc ctaccattct caggaggata 3000

gcgttaccga acatcgtggc aacagaagat tgagttttca ttcgcacaga attgaagaag 3060

ttcccaaaac agggctgggc tcctcggcag gtttagtcac agttttaact acagctttgg 3120

cctccttttt tgtatcggac ctggaaaata atgtagacaa atatagagaa gttattcata 3180

atttagcaca agttgctcat tgtcaagctc agggtaaaat tggaagcggg tttgatgtag 3240

cggcggcagc atatggatct atcagatata gaagattccc acccgcatta atctctaatt 3300

tgccagatat tggaagtgct acttacggca gtaaactggc gcatttggtt gatgaagaag 3360

actggaatat tacgattaaa agtaaccatt taccttcggg attaacttta tggatgggcg 3420

atattaagaa tggttcagaa acagtaaaac tggtccagaa ggtaaaaaat tggtatgatt 3480

cgcatatgcc agaaagcttg aaaatatata cagaactcga tcatgcaaat tctagattta 3540

tggatggact atctaaacta gatcgcttac acgagactca tgacgattac agcgatcaga 3600

tatttgagtc tcttgagagg aatgactgta cctgtcaaaa gtatcctgaa atcacagaag 3660

ttagagatgc agttgccaca attagacgtt cctttagaaa aataactaaa gaatctggtg 3720

ccgatatcga acctcccgta caaactagct tattggatga ttgccagacc ttaaaaggag 3780

ttcttacttg cttaatacct ggtgctggtg gttatgacgc cattgcagtg attactaagc 3840

aagatgttga tcttagggct caaaccgcta atgacaaaag attttctaag gttcaatggc 3900

tggatgtaac tcaggctgac tggggtgtta ggaaagaaaa agatccggaa acttatcttg 3960

ataaactgca ggaggagttt taatgtcatt accgttctta acttctgcac cgggaaaggt 4020

tattattttt ggtgaacact ctgctgtgta caacaagcct gccgtcgctg ctagtgtgtc 4080

tgcgttgaga acctacctgc taataagcga gtcatctgca ccagatacta ttgaattgga 4140

cttcccggac attagcttta atcataagtg gtccatcaat gatttcaatg ccatcaccga 4200

ggatcaagta aactcccaaa aattggccaa ggctcaacaa gccaccgatg gcttgtctca 4260

ggaactcgtt agtcttttgg atccgttgtt agctcaacta tccgaatcct tccactacca 4320

tgcagcgttt tgtttcctgt atatgtttgt ttgcctatgc ccccatgcca agaatattaa 4380

gttttcttta aagtctactt tacccatcgg tgctgggttg ggctcaagcg cctctatttc 4440

tgtatcactg gccttagcta tggcctactt gggggggtta ataggatcta atgacttgga 4500

aaagctgtca gaaaacgata agcatatagt gaatcaatgg gccttcatag gtgaaaagtg 4560

tattcacggt acccccttcag gaatagataa cgctgtggcc acttatggta atgccctgct 4620

atttgaaaaa gactcacata atggaacaat aaacacaaac aattttaagt tcttagatga 4680

tttcccagcc attccaatga tcctaaccta tactagaatt ccaaggtcta caaaagatct 4740

tgttgctcgc gttcgtgtgt tggtcaccga gaaatttcct gaagttatga agccaattct 4800

agatgccatg ggtgaatgtg ccctacaagg cttagagatc atgactaagt taagtaaatg 4860

taaaggcacc gatgacgagg ctgtagaaac taataatgaa ctgtatgaac aactattgga 4920

attgataaga ataaatcatg gactgcttgt ctcaatcggt gtttctcatc ctggattaga 4980
acttattaaa aatctgagcg atgatttgag aattggctcc acaaaactta ccggtgctgg 5040
tggcggcggt tgctctttga ctttgttacg aagagacatt actcaagagc aaattgacag 5100
cttcaaaaag aaattgcaag atgattttag ttacgagaca tttgaaacag acttgggtgg 5160
gactggctgc tgtttgttaa gcgcaaaaaa tttgaataaa gatcttaaaa tcaaatccct 5220
agtattccaa ttatttgaaa ataaaactac cacaaagcaa caaattgacg atctattatt 5280
gccaggaaac acgaatttac catggacttc agacgaggag ttttaatgac tgtatatact 5340
gctagtgtaa ctgctccggt aaatattgct actcttaagt attgggggaa aagggacacg 5400
aagttgaatc tgcccaccaa ttcgtccata tcagtgactt tatcgcaaga tgacctcaga 5460
acgttgacct ctgcggctac tgcacctgag tttgaacgcg acactttgtg gttaaatgga 5520
gaaccacaca gcatcgacaa tgaaagaact caaaattgtc tgcgcgacct acgccaatta 5580
agaaaggaaa tggaatcgaa ggacgcctca ttgcccacat tatctcaatg gaaactccac 5640
attgtctccg aaaataactt tcctacagca gctggtttag cttcctccgc tgctggcttt 5700
gctgcattgg tctctgcaat tgctaagtta taccaattac cacagtcaac ttcagaaata 5760
tctagaatag caagaaaggg gtctggttca gcttgtagat cgttgtttgg cggatacgtg 5820
gcctgggaaa tgggaaaagc tgaagatggt catgattcca tggcagtaca aatcgcagac 5880
agctctgact ggcctcagat gaaagcttgt gtcctagttg tcagcgatat taaaaaggat 5940
gtgagttcca ctcagggtat gcaattgacc gtggcaacct ccgaactatt taaagaaaga 6000
attgaacatg tcgtaccaaa gagatttgaa gtcatgcgta aagccattgt tgaaaaagat 6060
ttcgccacct ttgcaaagga aacaatgatg gattccaact ctttccatgc cacatgtttg 6120
gactctttcc ctccaatatt ctacatgaat gacacttcca agcgtatcat cagttggtgc 6180
cacaccatta atcagtttta cggagaaaca atcgttgcat acacgtttga tgcaggtcca 6240
aatgctgtgt tgtactactt agctgaaaat gagtcgaaac tctttgcatt tatctataaa 6300
ttgtttggct ctgttcctgg atgggacaag aaatttacta ctgagcagct tgaggctttc 6360
aaccatcaat ttgaatcatc taactttact gcacgtgaat tggatcttga gttgcaaaag 6420
gatgttgcca gagtgatttt aactcaagtc ggttcaggcc cacaagaaac aaacgaatct 6480
ttgattgacg caaagactgg tctaccaaag gaagaggagt tttaactcga cgccggcgga 6540
ggcacatatg tctcagaacg tttacattgt atcgactgcc agaaccccaa ttggttcatt 6600
ccagggttct ctatcctcca agacagcagt ggaattgggt gctgttgctt taaaaggcgc 6660
cttggctaag gttccagaat tggatgcatc caaggatttt gacgaaatta tttttggtaa 6720
cgttctttct gccaatttgg gccaagctcc ggccagacaa gttgctttgg ctgccggttt 6780
gagtaatcat atcgttgcaa gcacagttaa caaggtctgt gcatccgcta tgaaggcaat 6840

cattttgggt gctcaatcca tcaaatgtgg taatgctgat gttgtcgtag ctggtggttg 6900
tgaatctatg actaacgcac catactacat gccagcagcc cgtgcgggtg ccaaatttgg 6960
ccaaactgtt cttgttgatg gtgtcgaaag agatgggttg aacgatgcgt acgatggtct 7020
agccatgggt gtacacgcag aaaagtgtgc ccgtgattgg gatattacta gagaacaaca 7080
agacaatttt gccatcgaat cctaccaaaa atctcaaaaa tctcaaaagg aaggtaaatt 7140
cgacaatgaa attgtacctg ttaccattaa gggatttaga ggtaagcctg atactcaagt 7200
cacgaaggac gaggaacctg ctagattaca cgttgaaaaa ttgagatctg caaggactgt 7260
tttccaaaaa gaaaacggta ctgttactgc cgctaacgct tctccaatca acgatggtgc 7320
tgcagccgtc atcttggttt ccgaaaaagt tttgaaggaa aagaatttga agcctttggc 7380
tattatcaaa ggttggggtg aggccgctca tcaaccagct gattttacat gggctccatc 7440
tcttgcagtt ccaaaggctt tgaaacatgc tggcatcgaa gacatcaatt ctgttgatta 7500
ctttgaattc aatgaagcct tttcggttgt cggtttggtg aacactaaga ttttgaagct 7560
agacccatct aaggttaatg tatatggtgg tgctgttgct ctaggtcacc cattgggttg 7620
ttctggtgct agagtggttg ttacactgct atccatctta cagcaagaag gaggtaagat 7680
cggtgttgcc gccatttgta atggtggtgg tggtgcttcc tctattgtca ttgaaaagat 7740
atgaggatcc tctagatgcg caggaggcac atatggcgaa gaacgttggg attttggcta 7800
tggatatcta tttccctccc acctgtgttc aacaggaagc tttggaagca catgatggag 7860
caagtaaagg gaaatacact attggacttg gccaagattg tttagctttt tgcactgagc 7920
ttgaagatgt tatctctatg agtttcaatg cggtgacatc acttttgag aagtataaga 7980
ttgaccctaa ccaaatcggg cgtcttgaag taggaagtga gactgttatt gacaaaagca 8040
agtccatcaa gaccttcttg atgcagctct ttgagaaatg tggaaacact gatgtcgaag 8100
gtgttgactc gaccaatgct tgctatggtg gaactgcagc tttgttaaac tgtgtcaatt 8160
gggttgagag taactcttgg gatggacgtt atggcctcgt catttgtact gacagcgcgg 8220
tttatgcaga aggacccgca aggcccactg gaggagctgc agcgattgct atgttgatag 8280
gacctgatgc tcctatcgtt ttcgaaagca aattgagagc aagccacatg gctcatgtct 8340
atgactttta caagcccaat cttgctagcg agtacccggt tgttgatggt aagctttcac 8400
agacttgcta cctcatggct cttgactcct gctataaaca tttatgcaac aagttcgaga 8460
agatcgaggg caaagagttc tccataaatg atgctgatta cattgttttc cattctccat 8520
acaataaact tgtacagaaa agctttgctc gtctcttgta caacgacttc ttgagaaacg 8580
caagctccat tgacgaggct gccaaagaaa agttcacccc ttattcatct ttgacccttg 8640
acgagagtta ccaaagccgt gatcttgaaa aggtgtcaca acaaatttcg aaaccgtttt 8700
atgatgctaa agtgcaacca acgactttaa taccaaagga agtcggtaac atgtacactg 8760

cttctctcta cgctgcattt gcttccctca tccacaataa acacaatgat ttggcgggaa 8820
agcgggtggt tatgttctct tatggaagtg gctccaccgc aacaatgttc tcattacgcc 8880
tcaacgacaa taagcctcct ttcagcattt caaacattgc atctgtaatg gatgttggcg 8940
gtaaattgaa agctagacat gagtatgcac ctgagaagtt tgtggagaca atgaagctaa 9000
tggaacatag gtatggagca aaggactttg tgacaaccaa ggagggtatt atagatcttt 9060
tggcaccggg aacttattat ctgaaagagg ttgattcctt gtaccggaga ttctatggca 9120
agaaaggtga agatggatct gtagccaatg gacactgagg atccgtcgag cacgtggagg 9180
cacatatgca atgctgtgag atgcctgttg gatacattca gattcctgtt gggattgctg 9240
gtccattgtt gcttgatggt tatgagtact ctgttcctat ggctacaacc gaaggttgtt 9300
tggttgctag cactaacaga ggctgcaagg ctatgtttat ctctggtggc gccaccagta 9360
ccgttcttaa ggacggtatg acccgagcac ctgttgttcg gttcgcttcg gcgagacgag 9420
cttcggagct taagtttttc ttggagaatc cagagaactt tgatactttg gcagtagtct 9480
tcaacaggtc gagtagattt gcaagactgc aaagtgttaa atgcacaatc gcggggaaga 9540
atgcttatgt aaggttctgt tgtagtactg gtgatgctat ggggatgaat atggtttcta 9600
aaggtgtgca gaatgttctt gagtatctta ccgatgattt ccctgacatg gatgtgattg 9660
gaatctctgg taacttctgt tcggacaaga aacctgctgc tgtgaactgg attgagggac 9720
gtggtaaatc agttgtttgc gaggctgtaa tcagaggaga gatcgtgaac aaggtcttga 9780
aaacgagcgt ggctgcttta gtcgagctca acatgctcaa gaacctagct ggctctgctg 9840
ttgcaggctc tctaggtgga ttcaacgctc atgccagtaa catagtgtct gctgtattca 9900
tagctactgg ccaagatcca gctcaaaacg tggagagttc tcaatgcatc accatgatgg 9960
aagctattaa tgacggcaaa gatatccata tctcagtcac tatgccatct atcgaggtgg 10020
ggacagtggg aggaggaaca cagcttgcat ctcaatcagc gtgtttaaac ctgctcggag 10080
ttaaaggagc aagcacagag tcgccgggaa tgaacgcaag gaggctagcg acgatcgtag 10140
ccggagcagt tttagctgga gagttatctt taatgtcagc aattgcagct ggacagcttg 10200
tgagaagtca catgaaatac aatagatcca gccgagacat ctctggagca acgacaacga 10260
caacaacaac aacatgaccc gtaggaggca catatgagtt cccaacaaga gaaaaaggat 10320
tatgatgaag aacaattaag gttgatggaa gaagtttgta tcgttgtaga tgaaaatgat 10380
gtcoctttaa gatatggaac gaaaaaggag tgtcatttga tggaaaatat aaataaaggt 10440
cttttgcata gagcattctc tatgttcatc tttgatgagc aaaatcgcct tttacttcag 10500
cagcgtgcag aagagaaaat tacatttcca tccttatgga cgaatacatg ttgctcccac 10560
ccattggatg ttgctggtga acgtggtaat actttacctg aagctgttga aggtgttaag 10620
aatgcagctc aacgcaagct gttccatgaa ttgggtattc aagccaagta tattcccaaa 10680

gacaaatttc agtttcttac acgaatccat taccttgctc ctagtactgg tgcttgggga 10740
gagcatgaaa ttgactacat tcttttcttc aaaggtaaag ttgagctgga tatcaatccc 10800
aatgaagttc aagcctataa gtatgttact atggaagagt taaaagagat gttttccgat 10860
cctcaatatg gattcacacc atggttcaaa cttatttgtg agcattttat gtttaaatgg 10920
tggcaggatg tagatcatgc gtcaaaattc caagatacct taattcatcg ttgctaagga 10980
tcccccggga tccggccgat ctaaacaaac ccggaacaga ccgttgggaa gcgattcagt 11040
aattaaagct tcatgactcc tttttggttc ttaaagtccc tttgaggtat caactaataa 11100
gaaagatatt agacaacccc cctttttttct ttttcacaaa taggaagttt cgaatccaat 11160
ttggatatta aaaggattac cagatataac acaaaatctc tccacctatt ccttctagtc 11220
gagcctctcg gtctgtcatt atacctcgag aagtagaaag aattacaatc cccattccac 11280
ctaaaattcg cggaattcgt tgataattag aatagattcg tagaccaggt cgactgattc 11340
gttttaaatt taaaatattt ctatagggtc ttttcctatt ccttctatgt cgcagggtta 11400
aaaccaaaaa atatttgttt ttttctcgat gttttctcac gttttcgata aaaccttctc 11460
gtaaaagtat ttgaacaata ttttcggtaa tattagtaga tgctattcga accacccttt 11520
ttcgatccat atcagcattt cgtatagaag ttattatctc agcaatagtg tccctaccca 11580
tgatgaacta aaattattgg ggcctccaaa tttgatataa tcaacgtgtt ttttacttat 11640
ttttttttttg aatatgatat gaattattaa agatatatgc gtgagacaca atctactaat 11700
taatctattt ctttcaaata ccccactaga aacagatcac aatttcattt tataatacct 11760
cgggagctaa tgaaactatt ttagtaaaat ttaattctct caattcccgg gcgattgcac 11820
caaaaattcg agttcctttt gatttccttc cttcttgatc aataacaact gcagcattgt 11880
catcatatcg tattatcatc ccgttgtcac gtttgagttc tttacaggtc cgcacaatta 11940
cagctctgac tacttctgat ctttctaggg gcatatttgg tacggcttct ttgatcacag 12000
caacaataac gtcaccaata tgagcatatc gacgattgct agctcctatg attcgaatac 12060
acatcaattc tcgagccccg ctgttatccg ctacatttaa atgggtctga ggttgaatca 12120
ttttttttaat ccgttctttg aatgcaaagg gcgaagaaaa aaaagaaata tttttgtcca 12180
aaaaaaaaga aacatgcggt ttcgtttcat atctaagagc cctttccgca ttttttttcta 12240
ttacattacg aaataatgaa ttgagttcgt ataggcattt tagatgctgc tagtgaaata 12300
gcccttctgg ctatattttc tgttactcca cccatttcat aaagtattcg acccggttta 12360
acaacagcta cccaatattc aggggatcca ctagttctag agcggccgcc accgcggtgg 12420
agctccagct tttgttccct ttagtgaggg ttaatttcga gcttggcgta atcatggtca 12480
tagctgtttc ctgtgtgaaa ttgttatccg ctcacaattc cacacaacat acgagccgga 12540
agcataaagt gtaaagcctg gggtgcctaa tgagtgagct aactcacatt aattgcgttg 12600

cgctcactgc ccgctttcca gtcgggaaac ctgtcgtgcc agctgcatta atgaatcggc 12660
caacgcgcgg ggagaggcgg tttgcgtatt gggcgctctt ccgcttcctc gctcactgac 12720
tcgctgcgct cggtcgttcg gctgcggcga gcggtatcag ctcactcaaa ggcggtaata 12780
cggttatcca cagaatcagg ggataacgca ggaaagaaca tgtgagcaaa aggccagcaa 12840
aaggccagga accgtaaaaa ggccgcgttg ctggcgtttt tccataggct ccgcccccct 12900
gacgagcatc acaaaaatcg acgctcaagt cagaggtggc gaaacccgac aggactataa 12960
agataccagg cgtttccccc tggaagctcc ctcgtgcgct ctcctgttcc gaccctgccg 13020
cttaccggat acctgtccgc ctttctccct tcgggaagcg tggcgctttc tcatagctca 13080
cgctgtaggt atctcagttc ggtgtaggtc gttcgctcca agctgggctg tgtgcacgaa 13140
cccccgttc agcccgaccg ctgcgcctta tccggtaact atcgtcttga gtccaacccg 13200
gtaagacacg acttatcgcc actggcagca gccactggta acaggattag cagagcgagg 13260
tatgtaggcg gtgctacaga gttcttgaag tggtggccta actacggcta cactagaagg 13320
acagtatttg gtatctgcgc tctgctgaag ccagttacct tcggaaaaag agttggtagc 13380
tcttgatccg gcaaacaaac caccgctggt agcggtggtt tttttgtttg caagcagcag 13440
attacgcgca gaaaaaaagg atctcaagaa gatcctttga tcttttctac ggggtctgac 13500
gctcagtgga acgaaaactc acgttaaggg attttggtca tgagattatc aaaaaggatc 13560
ttcacctaga tcctttttaaa ttaaaaatga agttttaaat caatctaaag tatatatgag 13620
taaacttggt ctgacagtta ccaatgctta atcagtgagg cacctatctc agcgatctgt 13680
ctatttcgtt catccatagt tgcctgactc cccgtcgtgt agataactac gatacgggag 13740
ggcttaccat ctggccccag tgctgcaatg ataccgcgag acccacgctc accggctcca 13800
gatttatcag caataaacca gccagccgga agggccgagc gcagaagtgg tcctgcaact 13860
ttatccgcct ccatccagtc tattaattgt tgccgggaag ctagagtaag tagttcgcca 13920
gttaatagtt tgcgcaacgt tgttgccatt gctacaggca tcgtggtgtc acgctcgtcg 13980
tttggtatgg cttcattcag ctccggttcc caacgatcaa ggcgagttac atgatccccc 14040
atgttgtgca aaaaagcggt tagctccttc ggtcctccga tcgttgtcag aagtaagttg 14100
gccgcagtgt tatcactcat ggttatggca gcactgcata attctcttac tgtcatgcca 14160
tccgtaagat gcttttctgt gactggtgag tactcaacca agtcattctg agaatagtgt 14220
atgcggcgac cgagttgctc ttgcccggcg tcaatacggg ataataccgc gccacatagc 14280
agaactttaa aagtgctcat cattggaaaa cgttcttcgg ggcgaaaact ctcaaggatc 14340
ttaccgctgt tgagatccag ttcgatgtaa cccactcgtg cacccaactg atcttcagca 14400
tcttttactt tcaccagcgt ttctgggtga gcaaaaacag gaaggcaaaa tgccgcaaaa 14460
aagggaataa gggcgacacg gaaatgttga atactcatac tcttcctttt tcaatattat 14520

tgaagcattt atcagggtta ttgtctcatg agcggataca tatttgaatg tatttagaaa 14580

aataaacaaa taggggttcc gcgcacattt ccccgaaaag tgc 14623

<210> 75

<211> 7252

<212> DNA

<213> Artificial Sequence

<220>

<221> misc_feature

<222> ()..()

<223> Plastid transformation vector pFHO5 containing R. capsulatus DNA e

<400> 75

gcacttttcg gggaaatgtg cgcggaaccc ctatttgttt atttttctaa atacattcaa 60

atatgtatcc gctcatgaga caataaccct gataaatgct tcaataatat tgaaaaagga 120

agagtatgag tattcaacat ttccgtgtcg cccttattcc ctttttgcg gcattttgcc 180

ttcctgtttt tgctcaccca gaaacgctgg tgaaagtaaa agatgctgaa gatcagttgg 240

gtgcacgagt gggttacatc gaactggatc tcaacagcgg taagatcctt gagagttttc 300

gccccgaaga acgttttcca atgatgagca cttttaaagt tctgctatgt ggcgcggtat 360

tatcccgtat tgacgccggg caagagcaac tcggtcgccg catacactat tctcagaatg 420

acttggttga gtactcacca gtcacagaaa agcatcttac ggatggcatg acagtaagag 480

aattatgcag tgctgccata accatgagtg ataacactgc ggccaactta cttctgacaa 540

cgatcggagg accgaaggag ctaaccgctt ttttgcacaa catgggggat catgtaactc 600

gccttgatcg ttgggaaccg gagctgaatg aagccatacc aaacgacgag cgtgacacca 660

cgatgcctgt agcaatggca acaacgttgc gcaaactatt aactggcgaa ctacttactc 720

tagcttcccg gcaacaatta atagactgga tggaggcgga taaagttgca ggaccacttc 780

tgcgctcggc ccttccggct ggctggttta ttgctgataa atctggagcc ggtgagcgtg 840

ggtctcgcgg tatcattgca gcactggggc cagatggtaa gccctcccgt atcgtagtta 900

tctacacgac ggggagtcag gcaactatgg atgaacgaaa tagacagatc gctgagatag 960

gtgcctcact gattaagcat tggtaactgt cagaccaagt ttactcatat atactttaga 1020

ttgatttaaa acttcatttt taatttaaaa ggatctaggt gaagatcctt tttgataatc 1080

tcatgaccaa aatcccttaa cgtgagtttt cgttccactg agcgtcagac cccgtagaaa 1140

agatcaaagg atcttcttga gatccttttt ttctgcgcgt aatctgctgc ttgcaaacaa 1200

aaaaaccacc gctaccagcg gtggtttgtt tgccggatca agagctacca actcttttte 1260

cgaaggtaac tggcttcagc agagcgcaga taccaaatac tgtccttcta gtgtagccgt 1320

agttaggcca ccacttcaag aactctgtag caccgcctac atacctcgct ctgctaatcc 1380

tgttaccagt ggctgctgcc agtggcgata agtcgtgtct taccgggttg gactcaagac 1440

gatagttacc ggataaggcg cagcggtcgg gctgaacggg gggttcgtgc acacagccca 1500

gcttggagcg aacgacctac accgaactga gatacctaca gcgtgagcta tgagaaagcg 1560

ccacgcttcc cgaagggaga aaggcggaca ggtatccggt aagcggcagg gtcggaacag 1620

gagagcgcac gagggagctt ccagggggaa acgcctggta tctttatagt cctgtcgggt 1680

ttcgccacct ctgacttgag cgtcgatttt tgtgatgctc gtcaggggggg cggagcctat 1740

ggaaaaacgc cagcaacgcg gccttttac ggttcctggc cttttgctgg ccttttgctc 1800

acatgttctt tcctgcgtta tcccctgatt ctgtggataa ccgtattacc gcctttgagt 1860

gagctgatac cgctcgccgc agccgaacga ccgagcgcag cgagtcagtg agcgaggaag 1920

cggaagagcg cccaatacgc aaaccgcctc tccccgcgcg ttggccgatt cattaatgca 1980

gctggcacga caggtttccc gactggaaag cgggcagtga gcgcaacgca attaatgtga 2040

gttagctcac tcattaggca ccccaggctt tacactttat gcttccggct cgtatgttgt 2100

gtggaattgt gagcggataa caatttcaca caggaaacag ctatgaccat gattacgcca 2160

agctcgaaat taaccctcac taaagggaac aaaagctgga gctccaccgc ggtggcggcc 2220

gctctagaac tagtggatct tcttggctgt tattcaaaag gtccaacaat gtatatatat 2280

tggacatttt gaggcaatta tagatcctgg aaggcaattc tgattggtca ataaaaatcg 2340

atttcaatgc tatttttttt ttgtttttta tgagtttagc caatttatca tgaaaggtaa 2400

aaggggataa aggaaccgtg tgttgattgt cctgtaaata taagttgtct tcctccatat 2460

gtaaaaaggg aataaataaa tcaattaaat ttcgggatgc ttcatgaagt gcttctttcg 2520

gagttaaact tccgtttgtc catatttcga gaaaaagtat ctcttgtttt tcattcccat 2580

tcccataaga atgaatacta tgattcgcgt ttcgaacagg catgaataca gcatctatag 2640

gataacttcc atcttgaaag ttatgtggcg tttttataag atatccacga tttctctcta 2700

tttgtaatcc aatacaaaaa tcaattggtt ccgttaaact ggctatatgt tgtgtattat 2760

caacgatttc tacataaggc ggcaagatga tatcttgggc agttacagat ccaggaccct 2820

tgacacaaat agatgcgtca gaagttccat atagattact tcttaatata atttctttca 2880

aattcattaa aatttcatgt accgattctt gaatgcccgt tatggtagaa tattcatgtg 2940

ggactttctc agattttaca cgtgtgatac atgttccttc tatttctcca agtaaagctc 3000
ttcgcatcgc aatgcctatt gtgtcggctt ggcctttcat aagtggagac agaataaagc 3060
gtccataata aaggcgttta ctgtctgttc ttgattcaac acacttccac tgtagtgtcc 3120
gagtagatac tgttactttc tctcgaacca tagtactatt atttgattag atcatcgaat 3180
cttttatttc tcttgagatt tcttcaatgt tcagttctac acacgtcttt ttttcggagg 3240
tctacagcca ttatgtggca taggagttac atcccgtacg aaagttaata gtataccact 3300
tcgacgaata gctcgtaatg ctgcatctct tccgagaccg ggacctttta tcatgacttc 3360
tgctcgttgc ataccttgat ccactactgt acggatagcg tttgctgctg cggtttgagc 3420
agcaaacggt gttcctcttc tcgtaccttt gaatccagaa gtaccggcgg aggaccaaga 3480
aactactcga ccccgtacat ctgtaacagt gacaatggta ttattgaaac ttgcttgaac 3540
atgaataact ccctttggta ttctacgtgc acccttacgt gaaccaatac gtccattcct 3600
acgcgaacta attttcggta tagcttttgc catattttat catctcgtaa atatgagtca 3660
gagatatatg gatatatcca tttcatgtca aaacagattc tttatttgta catcggctct 3720
tctggcaagt ctgattatcc ctgtctttgt ttatgtctcg ggttggaaca aattactata 3780
attcgtcccc gcctacggat tagtcgacat ttttcacaaa ttttacgaac ggaagctctt 3840
attttcatat ttctcattcc ttaccttaat tctgaatcta tttcttggaa gaaaataagt 3900
ttcttgaaat ttttcatctc gaattgtatt cccacgaaag gaatggtgaa gttgaaaaac 3960
gaatccttca aatctttgtt gtggagtcga taaattatac gccctttggt tgaatcataa 4020
ggacttactt caattttgac tctatctcct ggcagtatcc gtataaaact atgccggatc 4080
tttcctgaaa cataatttat aatcagatcc aggaggacca tatgatcgcc gaagcggata 4140
tggaggtctg ccgggagctg atccgcaccg gcagctactc cttccatgcg gcgtccagag 4200
ttctgccggc gcgggtccgt gaccccgcgc tggcgcttta cgcctttgc cgcgtcgccg 4260
atgacgaagt cgacgaggtt ggcgcgccgc gcgacaaggc tgcggcggtt ttgaaacttg 4320
gcgaccggct ggaggacatc tatgccggtc gtccgcgcaa tgcgccctcg gatcgggctt 4380
tcgcggcggt ggtcgaggaa ttcgagatgc cgcgcgaatt gcccgaggcg ctgctggagg 4440
gcttcgcctg ggatgccgag gggcggtggt atcacacgct ttcggacgtg caggcctatt 4500
cggcgcgggt ggcggccgcc gtcggcgcga tgatgtgcgt gctgatgcgg gtgcgcaacc 4560
ccgatgcgct ggcgcgggcc tgcgatctcg gtcttgccat gcagatgtcg aacatcgccc 4620
gcgacgtggg cgaggatgcc cgggcggggc ggcttttcct gccgaccgac tggatggtcg 4680
aggaggggat cgatccgcag gcgttcctgg ccgatccgca gcccaccaag ggcatccgcc 4740
gggtcaccga gcggttgctg aaccgcgccg accggcttta ctggcgggcg gcgacggggg 4800
tgcggctttt gcccttgac tgccgaccgg ggatcatggc cgcgggcaag atctatgccg 4860

cgatcggggc cgaggtggcg aaggcgaaat acgacaacat cacccggcgt gcccacacga 4920
ccaagggccg caagctgtgg ctggtggcga attccgcgat gtcggcgacg gcgacctcga 4980
tgctgccgct ctcgccgcgg gtgcatgcca agcccgagcc cgaagtggcg catctggtcg 5040
atgccgccgc gcatcgcaac ctgcatcccg aacggtccga ggtgctgatc tcggcgctga 5100
tggcgctgaa ggcgcgcgac cgcggcctgg cgatggattg aggatctaaa caaacccgga 5160
acagaccgtt gggaagcgat tcagtaatta aagcttcatg actccttttt ggttcttaaa 5220
gtcoctttga ggtatcaact aataagaaag atattagaca acccccottt tttcttttc 5280
acaaatagga agtttcgaat ccaatttgga tattaaaagg attaccagat ataacacaaa 5340
atctctccac ctattccttc tagtcgagcc tctcggtctg tcattatacc tcgagaagta 5400
gaaagaatta caatccccat tccacctaaa attcgcggaa ttcgttgata attagaatag 5460
attcgtagac caggtcgact gattcgtttt aaatttaaaa tatttctata gggtcttttc 5520
ctattccttc tatgtcgcag ggttaaaacc aaaaaatatt tgtttttttc tcgatgtttt 5580
ctcacgtttt cgataaaacc ttctcgtaaa agtatttgaa caatattttc ggtaatatta 5640
gtagatgcta ttcgaaccac ccttttcga tccatatcag catttcgtat agaagttatt 5700
atctcagcaa tagtgtccct acccatgatg aactaaaatt attggggcct ccaaatttga 5760
tataatcaac gtgtttttta cttatttttt ttttgaatat gatatgaatt attaaagata 5820
tatgcgtgag acacaatcta ctaattaatc tatttctttc aaatacccca ctagaaacag 5880
atcacaattt cattttataa tacctcggga gctaatgaaa ctattttagt aaaatttaat 5940
tctctcaatt cccgggcgat tgcaccaaaa attcgagttc cttttgattt ccttccttct 6000
tgatcaataa caactgcagc attgtcatca tatcgtatta tcatcccgtt gtcacgtttg 6060
agttctttac aggtccgcac aattacagct ctgactactt ctgatctttc taggggcata 6120
tttggtacgg cttctttgat cacagcaaca ataacgtcac caatatgagc atatcgacga 6180
ttgctagctc ctatgattcg aatacacatc aattctcgag ccccgctgtt atccgctaca 6240
tttaaatggg tctgaggttg aatcattttt ttaatccgtt ctttgaatgc aaagggcgaa 6300
gaaaaaaaag aaatattttt gtccaaaaaa aaagaaacat gcggtttcgt ttcatatcta 6360
agagcccttt ccgcattttt ttctattaca ttacgaaata atgaattgag ttcgtatagg 6420
cattttagat gctgctagtg aaatagccct tctggctata ttttctgtta ctccacccat 6480
ttcataaagt attcgacccg gtttaacaac agctacccaa tattcagggg atcccccggg 6540
ctgcaggaat tcgatatcaa gcttatcgat accgtcgacc tcgaggggggg gcccggtacc 6600
caattcgccc tatagtgagt cgtattacaa ttcactggcc gtcgttttac aacgtcgtga 6660
ctgggaaaac cctggcgtta cccaacttaa tcgccttgca gcacatcccc ctttcgccag 6720
ctggcgtaat agcgaagagg cccgcaccga tcgcccttcc caacagttgc gcagcctgaa 6780

tggcgaatgg gacgcgccct gtagcggcgc attaagcgcg gcgggtgtgg tggttacgcg 6840

cagcgtgacc gctacacttg ccagcgccct agcgcccgct cctttcgctt tcttcccttc 6900

ctttctcgcc acgttcgccg gctttccccg tcaagctcta aatcgggggc tccctttagg 6960

gttccgattt agtgctttac ggcacctcga ccccaaaaaa cttgattagg gtgatggttc 7020

acgtagtggg ccatcgccct gatagacggt ttttcgccct ttgacgttgg agtccacgtt 7080

ctttaatagt ggactcttgt tccaaactgg aacaacactc aaccctatct cggtctattc 7140

ttttgattta taagggattt gccgatttc ggcctattgg ttaaaaaatg agctgattta 7200

acaaaaattt aacgcgaatt ttaacaaaat attaacgctt acaatttagg tg 7252

<210> 76

<211> 14623

<212> DNA

<213> Artificial Sequence

<220>

<221> misc_feature

<222> ()..()

<223> Plastid transformation vector pFHO6, containing Operon E, contain
i

<400> 76

cacctaaatt gtaagcgtta atattttgtt aaaattcgcg ttaaattttt gttaaatcag 60

ctcatttttt aaccaatagg ccgaaatcgg caaaatccct tataaatcaa aagaatagac 120

cgagataggg ttgagtgttg ttccagtttg gaacaagagt ccactattaa agaacgtgga 180

ctccaacgtc aaagggcgaa aaaccgtcta tcagggcgat ggcccactac gtgaaccatc 240

accctaatca agtttttttgg ggtcgaggtg ccgtaaagca ctaaatcgga accctaaagg 300

gagcccccga tttagagctt gacggggaaa gccggcgaac gtggcgagaa aggaagggaa 360

gaaagcgaaa ggagcgggcg ctagggcgct ggcaagtgta gcggtcacgc tgcgcgtaac 420

caccacaccc gccgcgctta atgcgccgct acagggcgcg tcccattcgc cattcaggct 480

gcgcaactgt tgggaagggc gatcggtgcg ggcctcttcg ctattacgcc agctggcgaa 540

aggggatgt gctgcaaggc gattaagttg ggtaacgcca gggttttccc agtcacgacg 600

ttgtaaaacg acggccagtg aattgtaata cgactcacta tagggcgaat tgggtaccgg 660

gccccccctc gaggtcgacg gtatcgataa gcttgatatc gaattcctgc agcccggggg 720

atcttcttgg ctgttattca aaaggtccaa caatgtatat atattggaca ttttgaggca 780

attatagatc ctggaaggca attctgattg gtcaataaaa atcgatttca atgctatttt 840

ttttttgttt tttatgagtt tagccaattt atcatgaaag gtaaaagggg ataaaggaac 900

cgtgtgttga ttgtcctgta aatataagtt gtcttcctcc atatgtaaaa agggaataaa 960

taaatcaatt aaatttcggg atgcttcatg aagtgcttct ttcggagtta aacttccgtt 1020

tgtccatatt tcgagaaaaa gtatctcttg tttttcattc ccattcccat aagaatgaat 1080

actatgattc gcgtttcgaa caggcatgaa tacagcatct ataggataac ttccatcttg 1140

aaagttatgt ggcgttttta taagatatcc acgatttctc tctatttgta atccaataca 1200

aaaatcaatt ggttccgtta aactggctat atgttgtgta ttatcaacga tttctacata 1260

aggcggcaag atgatatctt gggcagttac agatccagga cccttgacac aaatagatgc 1320

gtcagaagtt ccatatagat tacttcttaa tataatttct ttcaaattca ttaaaatttc 1380

atgtaccgat tcttgaatgc ccgttatggt agaatattca tgtgggactt tctcagattt 1440

tacacgtgtg atacatgttc cttctatttc tccaagtaaa gctcttcgca tcgcaatgcc 1500

tattgtgtcg gcttggcctt tcataagtgg agacagaata aagcgtccat aataaaggcg 1560

tttactgtct gttcttgatt caacacactt ccactgtagt gtccgagtag atactgttac 1620

tttctctcga accatagtac tattatttga ttagatcatc gaatctttta tttctcttga 1680

gatttcttca atgttcagtt ctacacacgt ctttttttcg gaggtctaca gccattatgt 1740

ggcataggag ttacatcccg tacgaaagtt aatagtatac cacttcgacg aatagctcgt 1800

aatgctgcat ctcttccgag accgggacct tttatcatga cttctgctcg ttgcatacct 1860

tgatccacta ctgtacggat agcgtttgct gctgcggttt gagcagcaaa cggtgttcct 1920

cttctcgtac ctttgaatcc agaagtaccg gcggaggacc aagaaactac tcgaccccgt 1980

acatctgtaa cagtgacaat ggtattattg aaacttgctt gaacatgaat aactcccttt 2040

ggtattctac gtgcaccctt acgtgaacca atacgtccat tcctacgcga actaattttc 2100

ggtatagctt ttgccatatt ttatcatctc gtaaatatga gtcagagata tatggatata 2160

tccatttcat gtcaaaacag attctttatt tgtacatcgg ctcttctggc aagtctgatt 2220

atccctgtct ttgtttatgt ctcgggttgg aacaaattac tataattcgt ccccgcctac 2280

ggattagtcg acatttttca caaattttac gaacggaagc tcttattttc atatttctca 2340

ttccttacct taattctgaa tctatttctt ggaagaaaat aagtttcttg aaatttttca 2400

tctcgaattg tattcccacg aaaggaatgg tgaagttgaa aaacgaatcc ttcaaatctt 2460

tgttgtggag tcgataaatt atacgccctt tggttgaatc ataaggactt acttcaattt 2520

tgactctatc tcctggcagt atccgtataa aactatgccg gatctttcct gaaacataat 2580

ttataatcag atcggccgca ggaggagttc atatgtcaga gttgagagcc ttcagtgccc 2640
cagggaaagc gttactagct ggtggatatt tagttttaga tacaaaatat gaagcatttg 2700
tagtcggatt atcggcaaga atgcatgctg tagcccatcc ttacggttca ttgcaagggt 2760
ctgataagtt tgaagtgcgt gtgaaaagta aacaatttaa agatggggag tggctgtacc 2820
atataagtcc taaaagtggc ttcattcctg tttcgatagg cggatctaag aacccttca 2880
ttgaaaaagt tatcgctaac gtatttagct actttaaacc taacatggac gactactgca 2940
atagaaactt gttcgttatt gatattttct ctgatgatgc ctaccattct caggaggata 3000
gcgttaccga acatcgtggc aacagaagat tgagttttca ttcgcacaga attgaagaag 3060
ttcccaaaac agggctgggc tcctcggcag gtttagtcac agttttaact acagctttgg 3120
cctccttttt tgtatcggac ctggaaaata atgtagacaa atatagagaa gttattcata 3180
atttagcaca agttgctcat tgtcaagctc agggtaaaat tggaagcggg tttgatgtag 3240
cggcggcagc atatggatct atcagatata gaagattccc acccgcatta atctctaatt 3300
tgccagatat tggaagtgct acttacggca gtaaactggc gcatttggtt gatgaagaag 3360
actggaatat tacgattaaa agtaaccatt taccttcggg attaacttta tggatgggcg 3420
atattaagaa tggttcagaa acagtaaaac tggtccagaa ggtaaaaaat tggtatgatt 3480
cgcatatgcc agaaagcttg aaaatatata cagaactcga tcatgcaaat tctagattta 3540
tggatggact atctaaacta gatcgcttac acgagactca tgacgattac agcgatcaga 3600
tatttgagtc tcttgagagg aatgactgta cctgtcaaaa gtatcctgaa atcacagaag 3660
ttagagatgc agttgccaca attagacgtt cctttagaaa aataactaaa gaatctggtg 3720
ccgatatcga acctcccgta caaactagct tattggatga ttgccagacc ttaaaaggag 3780
ttcttacttg cttaatacct ggtgctggtg gttatgacgc cattgcagtg attactaagc 3840
aagatgttga tcttagggct caaaccgcta atgacaaaag attttctaag gttcaatggc 3900
tggatgtaac tcaggctgac tggggtgtta ggaaagaaaa agatccggaa acttatcttg 3960
ataaactgca ggaggagttt taatgtcatt accgttctta acttctgcac cgggaaaggt 4020
tattattttt ggtgaacact ctgctgtgta caacaagcct gccgtcgctg ctagtgtgtc 4080
tgcgttgaga acctacctgc taataagcga gtcatctgca ccagatacta ttgaattgga 4140
cttcccggac attagcttta atcataagtg gtccatcaat gatttcaatg ccatcaccga 4200
ggatcaagta aactcccaaa aattggccaa ggctcaacaa gccaccgatg gcttgtctca 4260
ggaactcgtt agtcttttgg atccgttgtt agctcaacta tccgaatcct tccactacca 4320
tgcagcgttt tgtttcctgt atatgtttgt ttgcctatgc ccccatgcca agaatattaa 4380
gttttcttta aagtctactt tacccatcgg tgctgggttg ggctcaagcg cctctatttc 4440
tgtatcactg gccttagcta tggcctactt gggggggtta ataggatcta atgacttgga 4500

aaagctgtca gaaaacgata agcatatagt gaatcaatgg gccttcatag gtgaaaagtg 4560
tattcacggt acccccttcag gaatagataa cgctgtggcc acttatggta atgccctgct 4620
atttgaaaaa gactcacata atggaacaat aaacacaaac aattttaagt tcttagatga 4680
tttcccagcc attccaatga tcctaaccta tactagaatt ccaaggtcta caaaagatct 4740
tgttgctcgc gttcgtgtgt tggtcaccga gaaatttcct gaagttatga agccaattct 4800
agatgccatg ggtgaatgtg ccctacaagg cttagagatc atgactaagt taagtaaatg 4860
taaaggcacc gatgacgagg ctgtagaaac taataatgaa ctgtatgaac aactattgga 4920
attgataaga ataaatcatg gactgcttgt ctcaatcggt gtttctcatc ctggattaga 4980
acttattaaa aatctgagcg atgatttgag aattggctcc acaaaactta ccggtgctgg 5040
tggcggcggt tgctctttga ctttgttacg aagagacatt actcaagagc aaattgacag 5100
cttcaaaaag aaattgcaag atgattttag ttacgagaca tttgaaacag acttgggtgg 5160
gactggctgc tgtttgttaa gcgcaaaaaa tttgaataaa gatcttaaaa tcaaatccct 5220
agtattccaa ttatttgaaa ataaaactac cacaaagcaa caaattgacg atctattatt 5280
gccaggaaac acgaatttac catggacttc agacgaggag ttttaatgac tgtatatact 5340
gctagtgtaa ctgctccggt aaatattgct actcttaagt attgggggaa aagggacacg 5400
aagttgaatc tgcccaccaa ttcgtccata tcagtgactt tatcgcaaga tgacctcaga 5460
acgttgacct ctgcggctac tgcacctgag tttgaacgcg acactttgtg gttaaatgga 5520
gaaccacaca gcatcgacaa tgaaagaact caaaattgtc tgcgcgacct acgccaatta 5580
agaaaggaaa tggaatcgaa ggacgcctca ttgcccacat tatctcaatg gaaactccac 5640
attgtctccg aaaataactt tcctacagca gctggtttag cttcctccgc tgctggcttt 5700
gctgcattgg tctctgcaat tgctaagtta taccaattac cacagtcaac ttcagaaata 5760
tctagaatag caagaaaggg gtctggttca gcttgtagat cgttgtttgg cggatacgtg 5820
gcctgggaaa tgggaaaagc tgaagatggt catgattcca tggcagtaca aatcgcagac 5880
agctctgact ggcctcagat gaaagcttgt gtcctagttg tcagcgatat taaaaaggat 5940
gtgagttcca ctcagggtat gcaattgacc gtggcaacct ccgaactatt taaagaaaga 6000
attgaacatg tcgtaccaaa gagatttgaa gtcatgcgta aagccattgt tgaaaaagat 6060
ttcgccacct ttgcaaagga aacaatgatg gattccaact ctttccatgc cacatgtttg 6120
gactctttcc ctccaatatt ctacatgaat gacacttcca agcgtatcat cagttggtgc 6180
cacaccatta atcagtttta cggagaaaca atcgttgcat acacgtttga tgcaggtcca 6240
aatgctgtgt tgtactactt agctgaaaat gagtcgaaac tctttgcatt tatctataaa 6300
ttgtttggct ctgttcctgg atgggacaag aaatttacta ctgagcagct tgaggctttc 6360
aaccatcaat ttgaatcatc taactttact gcacgtgaat tggatcttga gttgcaaaag 6420

gatgttgcca gagtgatttt aactcaagtc ggttcaggcc cacaagaaac aaacgaatct 6480

ttgattgacg caaagactgg tctaccaaag gaagaggagt tttaactcga cgccggcgga 6540

ggcacatatg tctcagaacg tttacattgt atcgactgcc agaaccccaa ttggttcatt 6600

ccagggttct ctatcctcca agacagcagt ggaattgggt gctgttgctt taaaaggcgc 6660

cttggctaag gttccagaat tggatgcatc caaggatttt gacgaaatta tttttggtaa 6720

cgttctttct gccaatttgg gccaagctcc ggccagacaa gttgctttgg ctgccggttt 6780

gagtaatcat atcgttgcaa gcacagttaa caaggtctgt gcatccgcta tgaaggcaat 6840

cattttgggt gctcaatcca tcaaatgtgg taatgctgat gttgtcgtag ctggtggttg 6900

tgaatctatg actaacgcac catactacat gccagcagcc cgtgcgggtg ccaaatttgg 6960

ccaaactgtt cttgttgatg gtgtcgaaag agatgggttg aacgatgcgt acgatggtct 7020

agccatgggt gtacacgcag aaaagtgtgc ccgtgattgg gatattacta gagaacaaca 7080

agacaatttt gccatcgaat cctaccaaaa atctcaaaaa tctcaaaagg aaggtaaatt 7140

cgacaatgaa attgtacctg ttaccattaa gggatttaga ggtaagcctg atactcaagt 7200

cacgaaggac gaggaacctg ctagattaca cgttgaaaaa ttgagatctg caaggactgt 7260

tttccaaaaa gaaaacggta ctgttactgc cgctaacgct tctccaatca acgatggtgc 7320

tgcagccgtc atcttggttt ccgaaaaagt tttgaaggaa aagaatttga agcctttggc 7380

tattatcaaa ggttggggtg aggccgctca tcaaccagct gattttacat gggctccatc 7440

tcttgcagtt ccaaaggctt tgaaacatgc tggcatcgaa gacatcaatt ctgttgatta 7500

ctttgaattc aatgaagcct tttcggttgt cggtttggtg aacactaaga ttttgaagct 7560

agacccatct aaggttaatg tatatggtgg tgctgttgct ctaggtcacc cattgggttg 7620

ttctggtgct agagtggttg ttacactgct atccatctta cagcaagaag gaggtaagat 7680

cggtgttgcc gccatttgta atggtggtgg tggtgcttcc tctattgtca ttgaaaagat 7740

atgaggatcc tctagatgcg caggaggcac atatggcgaa gaacgttggg attttggcta 7800

tggatatcta tttccctccc acctgtgttc aacaggaagc tttggaagca catgatggag 7860

caagtaaagg gaaatacact attggacttg gccaagattg tttagctttt tgcactgagc 7920

ttgaagatgt tatctctatg agtttcaatg cggtgacatc acttttgag aagtataaga 7980

ttgaccctaa ccaaatcggg cgtcttgaag taggaagtga gactgttatt gacaaaagca 8040

agtccatcaa gaccttcttg atgcagctct ttgagaaatg tggaaacact gatgtcgaag 8100

gtgttgactc gaccaatgct tgctatggtg gaactgcagc tttgttaaac tgtgtcaatt 8160

gggttgagag taactcttgg gatggacgtt atggcctcgt catttgtact gacagcgcgg 8220

tttatgcaga aggacccgca aggcccactg gaggagctgc agcgattgct atgttgatag 8280

gacctgatgc tcctatcgtt ttcgaaagca aattgagagc aagccacatg gctcatgtct 8340

atgactttta caagcccaat cttgctagcg agtacccggt tgttgatggt aagctttcac 8400
agacttgcta cctcatggct cttgactcct gctataaaca tttatgcaac aagttcgaga 8460
agatcgaggg caaagagttc tccataaatg atgctgatta cattgttttc cattctccat 8520
acaataaact tgtacagaaa agctttgctc gtctcttgta caacgacttc ttgagaaacg 8580
caagctccat tgacgaggct gccaaagaaa agttcacccc ttattcatct ttgacccttg 8640
acgagagtta ccaaagccgt gatcttgaaa aggtgtcaca acaaatttcg aaaccgtttt 8700
atgatgctaa agtgcaacca acgactttaa taccaaagga agtcggtaac atgtacactg 8760
cttctctcta cgctgcattt gcttccctca tccacaataa acacaatgat ttggcgggaa 8820
agcgggtggt tatgttctct tatggaagtg gctccaccgc aacaatgttc tcattacgcc 8880
tcaacgacaa taagcctcct ttcagcattt caaacattgc atctgtaatg gatgttggcg 8940
gtaaattgaa agctagacat gagtatgcac ctgagaagtt tgtggagaca atgaagctaa 9000
tggaacatag gtatggagca aaggactttg tgacaaccaa ggagggtatt atagatcttt 9060
tggcaccggg aacttattat ctgaaagagg ttgattcctt gtaccggaga ttctatggca 9120
agaaaggtga agatggatct gtagccaatg gacactgagg atccgtcgag cacgtggagg 9180
cacatatgca atgctgtgag atgcctgttg gatacattca gattcctgtt gggattgctg 9240
gtccattgtt gcttgatggt tatgagtact ctgttcctat ggctacaacc gaaggttgtt 9300
tggttgctag cactaacaga ggctgcaagg ctatgtttat ctctggtggc gccaccagta 9360
ccgttcttaa ggacggtatg acccgagcac ctgttgttcg gttcgcttcg gcgagacgag 9420
cttcggagct taagtttttc ttggagaatc cagagaactt tgatactttg gcagtagtct 9480
tcaacaggtc gagtagattt gcaagactgc aaagtgttaa atgcacaatc gcggggaaga 9540
atgcttatgt aaggttctgt tgtagtactg gtgatgctat ggggatgaat atggtttcta 9600
aaggtgtgca gaatgttctt gagtatctta ccgatgattt ccctgacatg gatgtgattg 9660
gaatctctgg taacttctgt tcggacaaga aacctgctgc tgtgaactgg attgagggac 9720
gtggtaaatc agttgtttgc gaggctgtaa tcagaggaga gatcgtgaac aaggtcttga 9780
aaacgagcgt ggctgcttta gtcgagctca acatgctcaa gaacctagct ggctctgctg 9840
ttgcaggctc tctaggtgga ttcaacgctc atgccagtaa catagtgtct gctgtattca 9900
tagctactgg ccaagatcca gctcaaaacg tggagagttc tcaatgcatc accatgatgg 9960
aagctattaa tgacggcaaa gatatccata tctcagtcac tatgccatct atcgaggtgg 10020
ggacagtggg aggaggaaca cagcttgcat ctcaatcagc gtgtttaaac ctgctcggag 10080
ttaaaggagc aagcacagag tcgccgggaa tgaacgcaag gaggctagcg acgatcgtag 10140
ccggagcagt tttagctgga gagttatctt taatgtcagc aattgcagct ggacagcttg 10200
tgagaagtca catgaaatac aatagatcca gccgagacat ctctggagca acgacaacga 10260

caacaacaac aacatgaccc gtaggaggca catatgagtt cccaacaaga gaaaaaggat 10320
tatgatgaag aacaattaag gttgatggaa gaagtttgta tcgttgtaga tgaaaatgat 10380
gtccctttaa gatatggaac gaaaaaggag tgtcatttga tggaaaatat aaataaaggt 10440
cttttgcata gagcattctc tatgttcatc tttgatgagc aaaatcgcct tttacttcag 10500
cagcgtgcag aagagaaaat tacatttcca tccttatgga cgaatacatg ttgctcccac 10560
ccattggatg ttgctggtga acgtggtaat actttacctg aagctgttga aggtgttaag 10620
aatgcagctc aacgcaagct gttccatgaa ttgggtattc aagccaagta tattcccaaa 10680
gacaaatttc agtttcttac acgaatccat taccttgctc ctagtactgg tgcttgggga 10740
gagcatgaaa ttgactacat tcttttcttc aaaggtaaag ttgagctgga tatcaatccc 10800
aatgaagttc aagcctataa gtatgttact atggaagagt taaaagagat gttttccgat 10860
cctcaatatg gattcacacc atggttcaaa cttatttgtg agcattttat gtttaaatgg 10920
tggcaggatg tagatcatgc gtcaaaattc caagatacct taattcatcg ttgctaagga 10980
tcccccggga tccggccgat ctaaacaaac ccggaacaga ccgttgggaa gcgattcagt 11040
aattaaagct tcatgactcc tttttggttc ttaaagtccc tttgaggtat caactaataa 11100
gaaagatatt agacaacccc ccttttttct ttttcacaaa taggaagttt cgaatccaat 11160
ttggatatta aaaggattac cagatataac acaaaatctc tccacctatt ccttctagtc 11220
gagcctctcg gtctgtcatt atacctcgag aagtagaaag aattacaatc cccattccac 11280
ctaaaattcg cggaattcgt tgataattag aatagattcg tagaccaggt cgactgattc 11340
gttttaaatt taaaatattt ctatagggtc ttttcctatt ccttctatgt cgcagggtta 11400
aaaccaaaaa atatttgttt ttttctcgat gttttctcac gttttcgata aaaccttctc 11460
gtaaaagtat ttgaacaata ttttcggtaa tattagtaga tgctattcga accacccttt 11520
ttcgatccat atcagcattt cgtatagaag ttattatctc agcaatagtg tccctaccca 11580
tgatgaacta aaattattgg ggcctccaaa tttgatataa tcaacgtgtt ttttacttat 11640
ttttttttg aatatgatat gaattattaa agatatatgc gtgagacaca atctactaat 11700
taatctattt ctttcaaata ccccactaga aacagatcac aatttcattt tataatacct 11760
cgggagctaa tgaaactatt ttagtaaaat ttaattctct caattcccgg gcgattgcac 11820
caaaaattcg agttcctttt gatttccttc cttcttgatc aataacaact gcagcattgt 11880
catcatatcg tattatcatc ccgttgtcac gtttgagttc tttacaggtc cgcacaatta 11940
cagctctgac tacttctgat ctttctaggg gcatatttgg tacggcttct ttgatcacag 12000
caacaataac gtcaccaata tgagcatatc gacgattgct agctcctatg attcgaatac 12060
acatcaattc tcgagccccg ctgttatccg ctacatttaa atgggtctga ggttgaatca 12120
ttttttaat ccgttctttg aatgcaaagg gcgaagaaaa aaaagaaata tttttgtcca 12180

aaaaaaaaga aacatgcggt ttcgtttcat atctaagagc cctttccgca ttttttttcta 12240
ttacattacg aaataatgaa ttgagttcgt ataggcattt tagatgctgc tagtgaaata 12300
gcccttctgg ctatattttc tgttactcca cccatttcat aaagtattcg acccggttta 12360
acaacagcta cccaatattc aggggatcca ctagttctag agcggccgcc accgcggtgg 12420
agctccagct tttgttccct ttagtgaggg ttaatttcga gcttggcgta atcatggtca 12480
tagctgtttc ctgtgtgaaa ttgttatccg ctcacaattc cacacaacat acgagccgga 12540
agcataaagt gtaaagcctg gggtgcctaa tgagtgagct aactcacatt aattgcgttg 12600
cgctcactgc ccgctttcca gtcgggaaac ctgtcgtgcc agctgcatta atgaatcggc 12660
caacgcgcgg ggagaggcgg tttgcgtatt gggcgctctt ccgcttcctc gctcactgac 12720
tcgctgcgct cggtcgttcg gctgcggcga gcggtatcag ctcactcaaa ggcggtaata 12780
cggttatcca cagaatcagg ggataacgca ggaaagaaca tgtgagcaaa aggccagcaa 12840
aaggccagga accgtaaaaa ggccgcgttg ctggcgtttt tccataggct ccgcccccct 12900
gacgagcatc acaaaaatcg acgctcaagt cagaggtggc gaaacccgac aggactataa 12960
agataccagg cgtttccccc tggaagctcc ctcgtgcgct ctcctgttcc gaccctgccg 13020
cttaccggat acctgtccgc ctttctccct tcgggaagcg tggcgctttc tcatagctca 13080
cgctgtaggt atctcagttc ggtgtaggtc gttcgctcca agctgggctg tgtgcacgaa 13140
cccccgttc agcccgaccg ctgcgcctta tccggtaact atcgtcttga gtccaacccg 13200
gtaagacacg acttatcgcc actggcagca gccactggta acaggattag cagagcgagg 13260
tatgtaggcg gtgctacaga gttcttgaag tggtggccta actacggcta cactagaagg 13320
acagtatttg gtatctgcgc tctgctgaag ccagttacct tcggaaaaag agttggtagc 13380
tcttgatccg gcaaacaaac caccgctggt agcggtggtt tttttgtttg caagcagcag 13440
attacgcgca gaaaaaaagg atctcaagaa gatcctttga tcttttctac ggggtctgac 13500
gctcagtgga acgaaaactc acgttaaggg attttggtca tgagattatc aaaaaggatc 13560
ttcacctaga tccttttaaa ttaaaaatga agttttaaat caatctaaag tatatatgag 13620
taaacttggt ctgacagtta ccaatgctta atcagtgagg cacctatctc agcgatctgt 13680
ctatttcgtt catccatagt tgcctgactc cccgtcgtgt agataactac gatacgggag 13740
ggcttaccat ctggccccag tgctgcaatg ataccgcgag acccacgctc accggctcca 13800
gatttatcag caataaacca gccagccgga agggccgagc gcagaagtgg tcctgcaact 13860
ttatccgcct ccatccagtc tattaattgt tgccgggaag ctagagtaag tagttcgcca 13920
gttaatagtt tgcgcaacgt tgttgccatt gctacaggca tcgtggtgtc acgctcgtcg 13980
tttggtatgg cttcattcag ctccggttcc caacgatcaa ggcgagttac atgatccccc 14040
atgttgtgca aaaaagcggt tagctccttc ggtcctccga tcgttgtcag aagtaagttg 14100

gccgcagtgt tatcactcat ggttatggca gcactgcata attctcttac tgtcatgcca 14160

tccgtaagat gcttttctgt gactggtgag tactcaacca agtcattctg agaatagtgt 14220

atgcggcgac cgagttgctc ttgcccggcg tcaatacggg ataataccgc gccacatagc 14280

agaactttaa aagtgctcat cattggaaaa cgttcttcgg ggcgaaaact ctcaaggatc 14340

ttaccgctgt tgagatccag ttcgatgtaa cccactcgtg cacccaactg atcttcagca 14400

tcttttactt tcaccagcgt ttctgggtga gcaaaaacag gaaggcaaaa tgccgcaaaa 14460

aagggaataa gggcgacacg gaaatgttga atactcatac tcttcctttt tcaatattat 14520

tgaagcattt atcagggtta ttgtctcatg agcggataca tatttgaatg tatttagaaa 14580

aataaacaaa taggggttcc gcgcacattt ccccgaaaag tgc 14623